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=> fil reg
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STRUCTURE FILE UPDATES:   26 SEP 2005  HIGHEST RN 863963-04-6
DICTIONARY FILE UPDATES:  26 SEP 2005  HIGHEST RN 863963-04-6

New CAS Information Use Policies, enter HELP USAGETERMS for details.

TSCA INFORMATION NOW CURRENT THROUGH JULY 14, 2005

  Please note that search-term pricing does apply when
  conducting SmartSELECT searches.

**********************************************************************
*                                                                    *
* The CA roles and document type information have been removed from *
* the IDE default display format and the ED field has been added,   *
* effective March 20, 2005.  A new display format, IDERL, is now    *
* available and contains the CA role and document type information. *
*                                                                    *
**********************************************************************

Structure search iteration limits have been increased.  See HELP SLIMITS
for details.

Experimental and calculated property data are now available. For more
information enter HELP PROP at an arrow prompt in the file or refer
to the file summary sheet on the web at:
http://www.cas.org/ONLINE/DBSS/registryss.html

=> d sqide can tot l25

L25  ANSWER 1 OF 23  REGISTRY  COPYRIGHT 2005 ACS on STN
RN   740808-64-4  REGISTRY
CN   L-Arginine, D-arginyl-L-arginyl-L-prolyl-L-prolylglycyl-L-phenylalanyl-L-
     seryl-(3R)-1,2,3,4-tetrahydro-3-isoquinolinecarbonyloctahydro-1H-indole-2-
     carbonyl- (9CI)  (CA INDEX NAME)
FS   PROTEIN SEQUENCE; STEREOSEARCH
SQL  10
NTE
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 type            ------ location ------         description
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uncommon         Tic-8           -         -
uncommon         Oic-9           -         -
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SEQ      1 RRPPGFSXXR

**RELATED SEQUENCES AVAILABLE WITH SEQLINK**
MF   C61 H91 N19 O12
SR   CA
LC   STN Files:   CA, CAPLUS, USPATFULL
DT.CA  CAplus document type:  Patent
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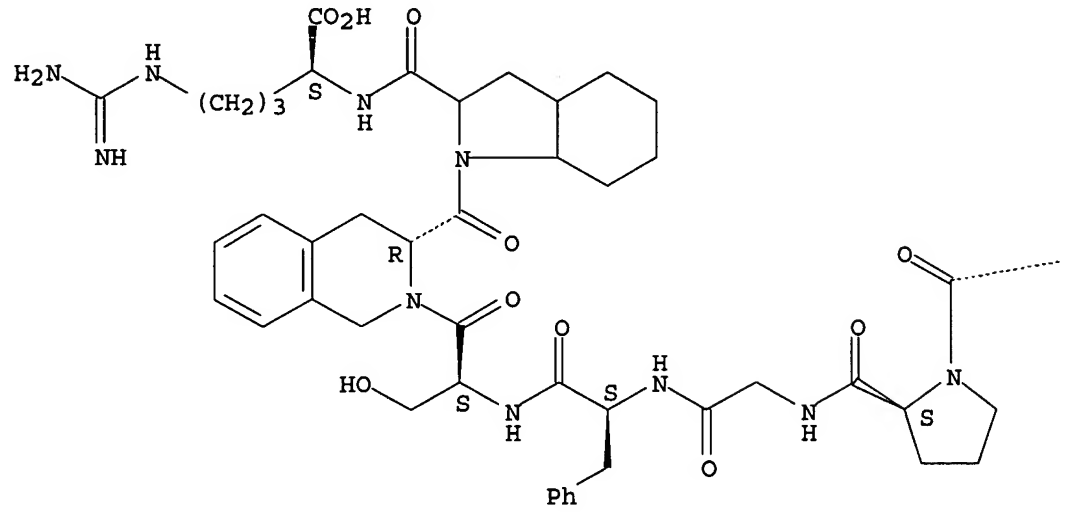
RL.P Roles from patents: BIOL (Biological study); PRP (Properties); USES (Uses)

Absolute stereochemistry.

PAGE 1-A



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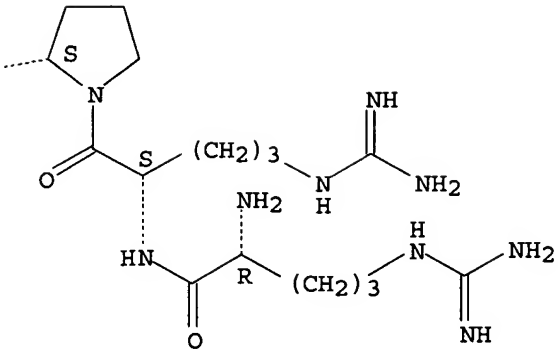

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 141:185137

L25 ANSWER 2 OF 23 REGISTRY COPYRIGHT 2005 ACS on STN
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uncommon	Tic-8	-	-
uncommon	Oic-9	-	-

SEQ 1 RRXPGFSXXR

RELATED SEQUENCES AVAILABLE WITH SEQLINK
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LC STN Files: CA, CAPLUS, USPATFULL
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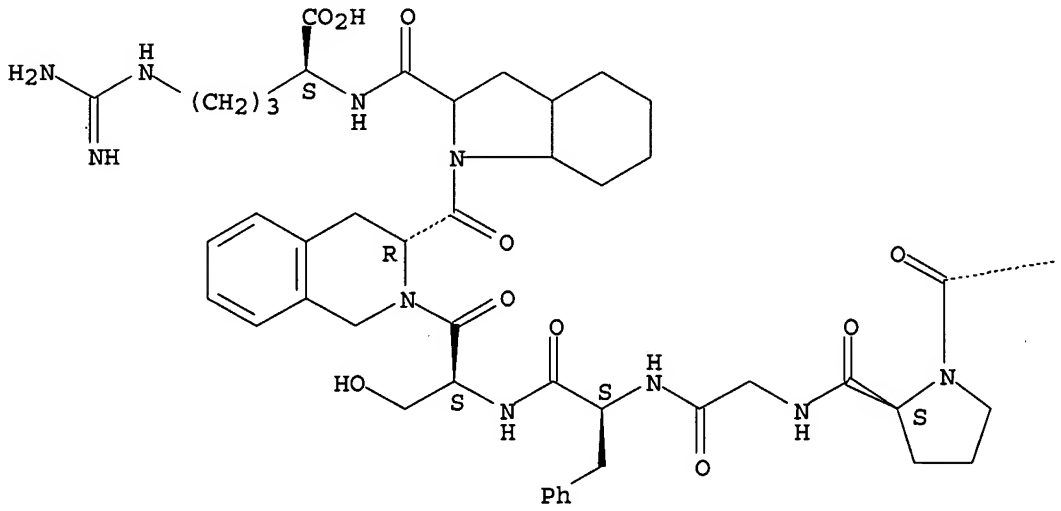
RL.P Roles from patents: BIOL (Biological study); PRP (Properties); USES (Uses)

Absolute stereochemistry.

PAGE 1-A



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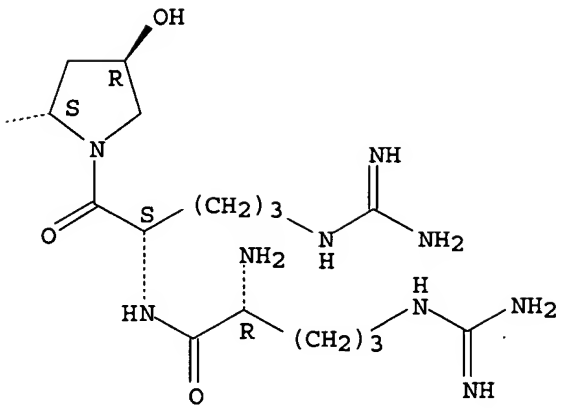

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

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1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 141:185137

L25 ANSWER 3 OF 23 REGISTRY COPYRIGHT 2005 ACS on STN
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uncommon	Tic-8	-	-
uncommon	Oic-9	-	-

SEQ 1 RRPXGFSXXR

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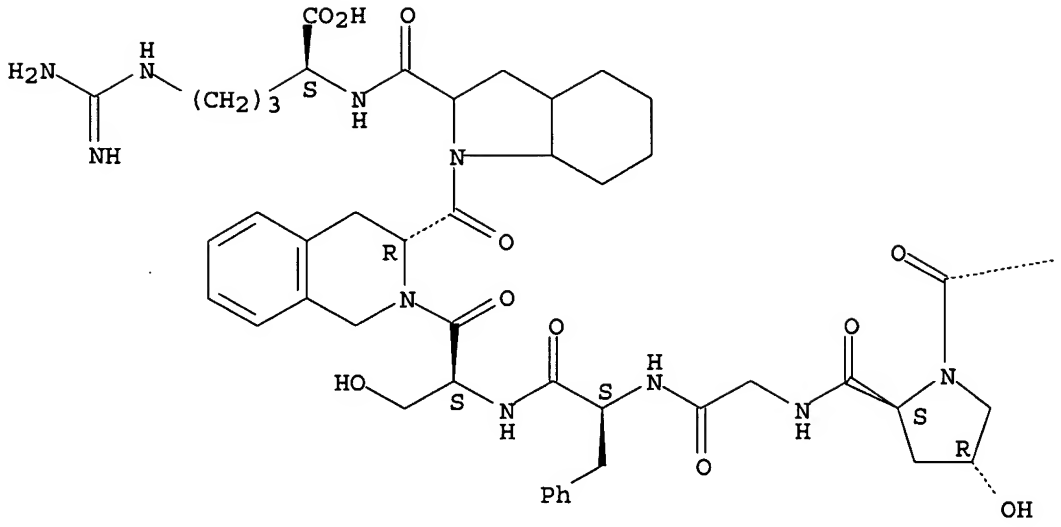
SR CA
LC STN Files: CA, CAPLUS, USPATFULL
DT.CA CAplus document type: Patent
RL.P Roles from patents: BIOL (Biological study); PRP (Properties); USES (Uses)

Absolute stereochemistry.

PAGE 1-A



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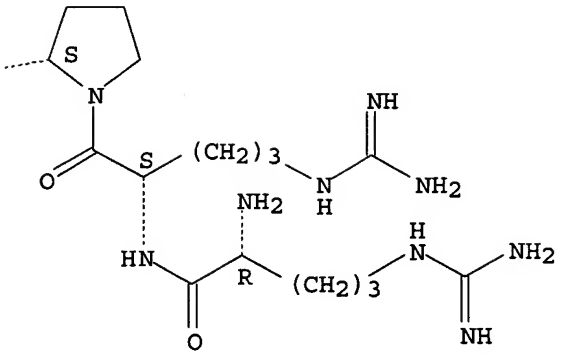

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1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 141:185137

L25 ANSWER 4 OF 23 REGISTRY COPYRIGHT 2005 ACS on STN
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isoquinolinecarbonyloctahydro-1H-indole-2-carbonyl- (9CI) (CA INDEX NAME)
FS PROTEIN SEQUENCE; STEREOSEARCH
SQL **10**
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uncommon	Thi-6	-	-
uncommon	Tic-8	-	-
uncommon	Oic-9	-	-

SEQ 1 RRPPGXSXXR

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MF C59 H89 N19 O12 S
SR CA
LC STN Files: CA, CAPLUS, USPATFULL
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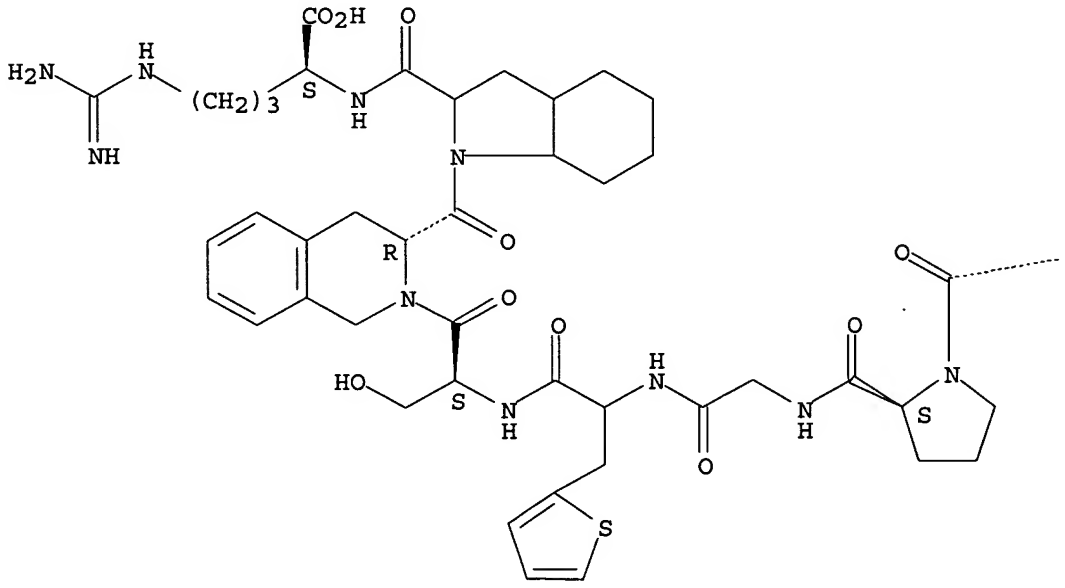
RL.P Roles from patents: BIOL (Biological study); PRP (Properties); USES (Uses)

Absolute stereochemistry.

PAGE 1-A



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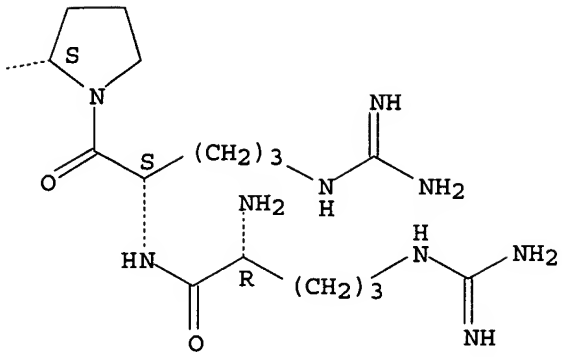

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 141:185137

L25 ANSWER 5 OF 23 REGISTRY COPYRIGHT 2005 ACS on STN
RN 603969-58-0 REGISTRY
CN L-Arginine, D-arginyl-L-arginyl-L-prolyl-(4R)-4-hydroxy-L-prolylglycyl-3-(2-thienyl)-L-alanyl-L-seryl-(3S)-1,2,3,4-tetrahydro-3-isoquinolinecarbonyl-(2S,3aS,7aS)-octahydro-1H-indole-2-carbonyl- (9CI) (CA INDEX NAME)
OTHER NAMES:
CN 195: PN: US20030176421 PAGE: 54-55 claimed sequence
FS PROTEIN SEQUENCE; STEREOSEARCH
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uncommon	Thi-6	-	-
uncommon	Tic-8	-	-
uncommon	Oic-9	-	-

PATENT ANNOTATIONS (PNTE):

Sequence Source	Patent Reference
Not Given	US2003176421 claimed PAGE 54-55

SEQ 1 RRPXGXSXXR

RELATED SEQUENCES AVAILABLE WITH SEQLINK
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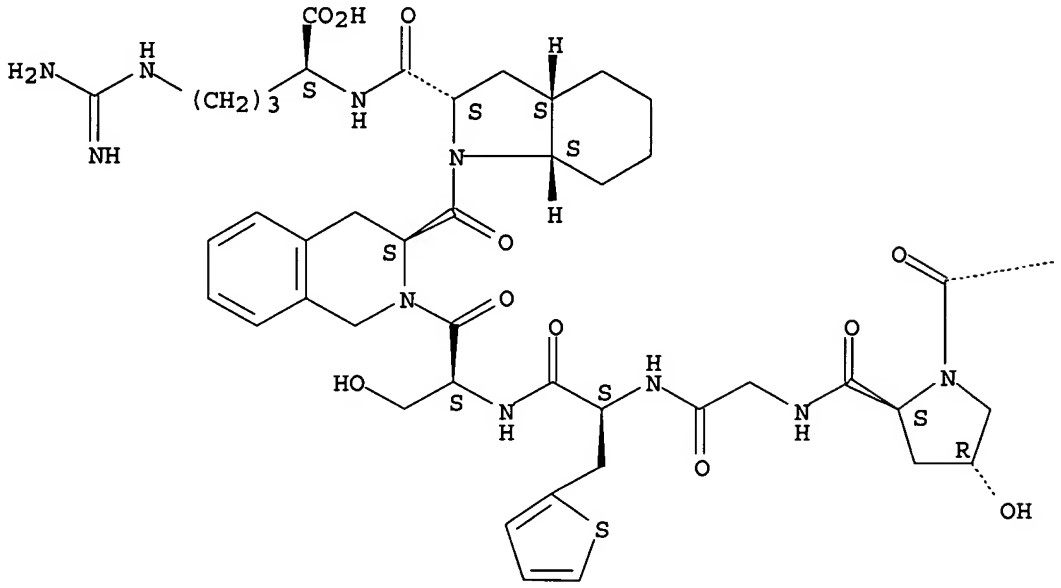
RL.P Roles from patents: BIOL (Biological study); PRP (Properties); USES (Uses)

Absolute stereochemistry.

PAGE 1-A



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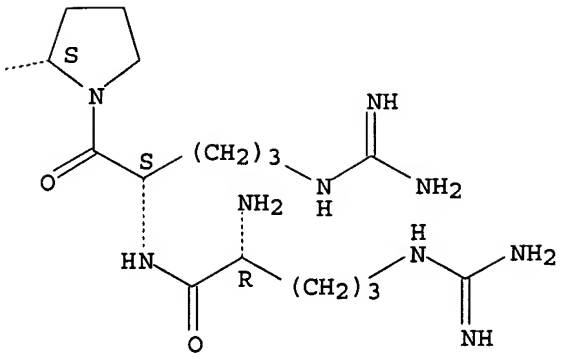

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1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 139:255368

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uncommon	Tic-8	-	-
uncommon	Oic-9	-	-

SEQ 1 RRPXGXSXXR

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LC STN Files: CA, CAPLUS, USPATFULL
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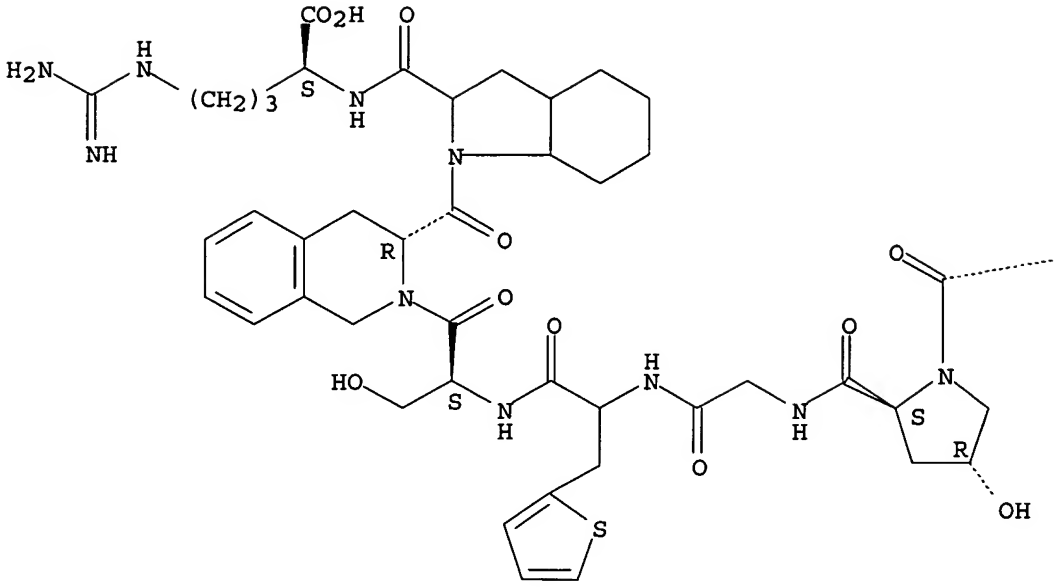
Absolute stereochemistry.

PAGE 1-A



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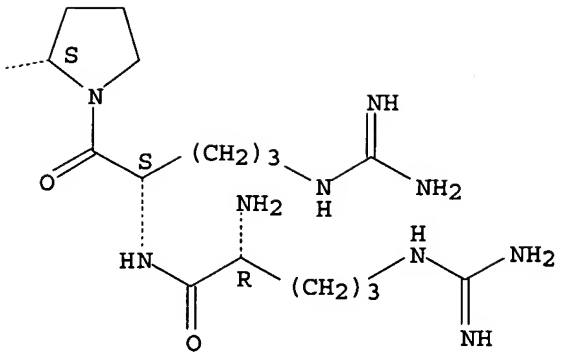

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 141:185137

L25 ANSWER 7 OF 23 REGISTRY COPYRIGHT 2005 ACS on STN
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isoquinolinecarbonyl-(2S,3aS,7aR)-octahydro-1H-indole-2-carbonyl- (9CI) (CA INDEX NAME)
FS PROTEIN SEQUENCE; STEREOSEARCH
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SEQ 1 RRPXGXSXXR

RELATED SEQUENCES AVAILABLE WITH SEQLINK
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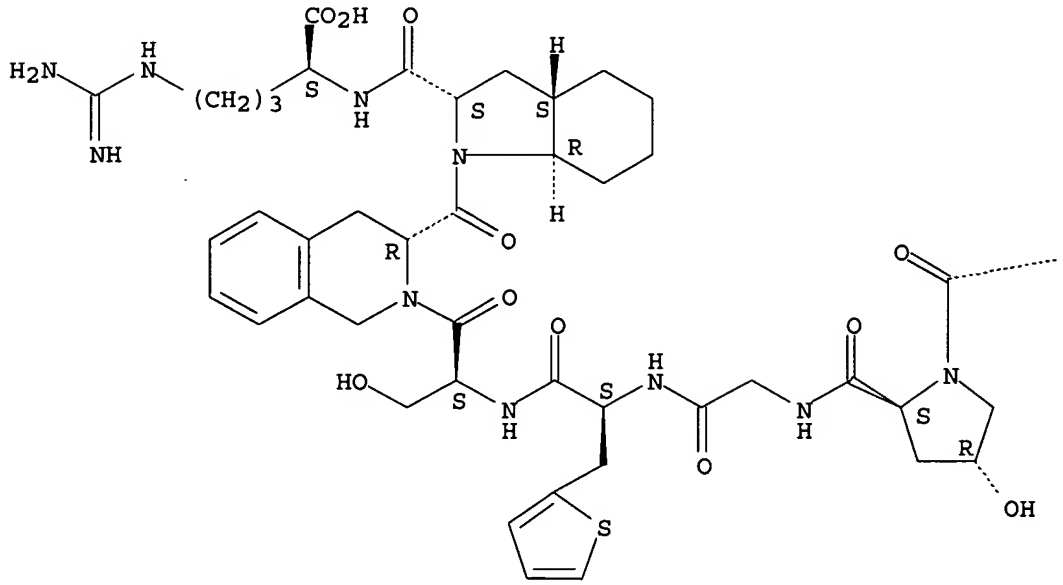
SR CA
LC STN Files: CA, CAPLUS, USPATFULL
DT.CA CAplus document type: Patent
RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); USES (Uses)

Absolute stereochemistry.

PAGE 1-A



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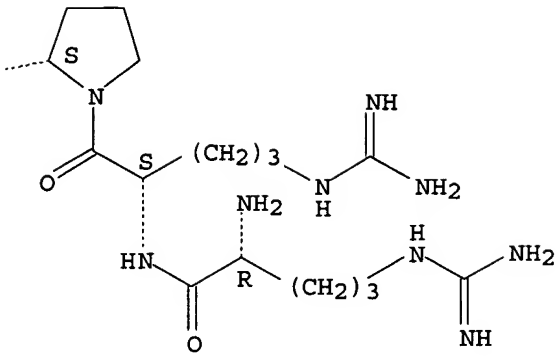

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 127:162123

L25 ANSWER 8 OF 23 REGISTRY COPYRIGHT 2005 ACS on STN
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FS PROTEIN SEQUENCE; STEREOSEARCH
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uncommon	Thi-6	-	-
uncommon	Tic-8	-	-
uncommon	Oic-9	-	-

SEQ 1 RRPXGXSXXR

RELATED SEQUENCES AVAILABLE WITH SEQLINK
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SR CA
LC STN Files: CA, CAPLUS, CASREACT, USPATFULL
DT.CA CAplus document type: Journal; Patent
RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); USES (Uses)
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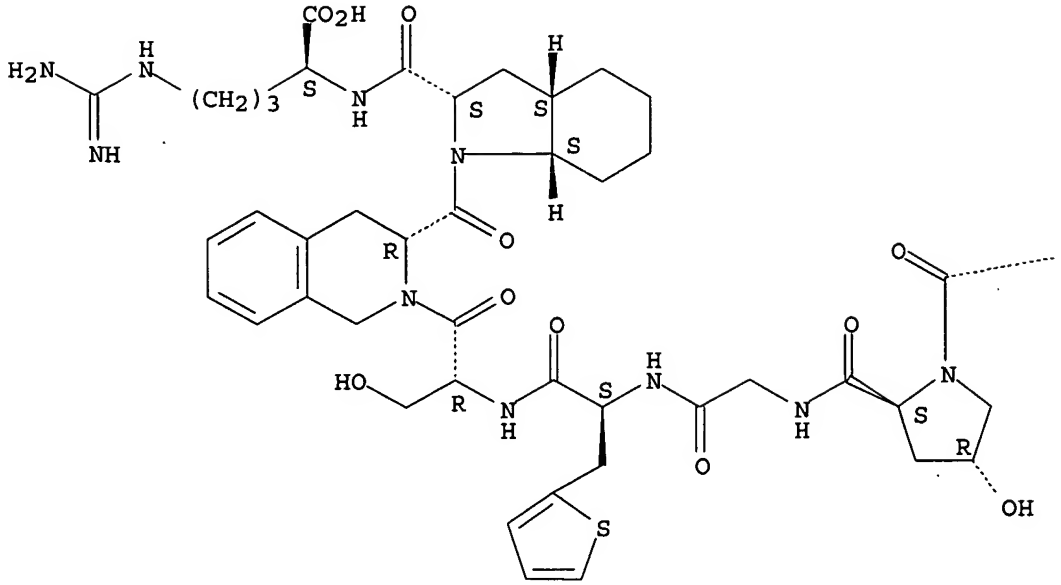
Absolute stereochemistry.

PAGE 1-A



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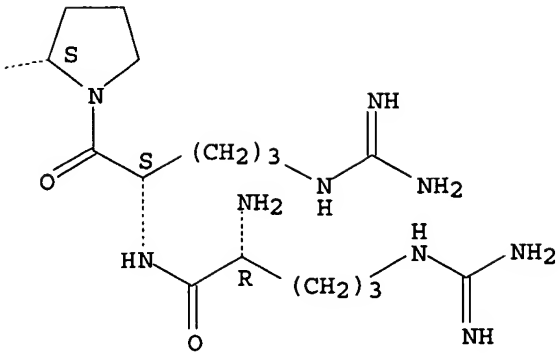

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2 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 134:163320

REFERENCE 2: 127:162123

L25 ANSWER 9 OF 23 REGISTRY COPYRIGHT 2005 ACS on STN
RN 193618-63-2 REGISTRY
CN L-Arginine, D-arginyl-L-arginyl-L-prolyl-(4R)-4-hydroxy-L-prolylglycyl-3-

(2-thienyl)-D-alanyl-L-seryl-(3R)-1,2,3,4-tetrahydro-3-isoquinolinecarbonyl-(2S,3aS,7aS)-octahydro-1H-indole-2-carbonyl- (9CI) (CA INDEX NAME)

FS PROTEIN SEQUENCE; STEREOSEARCH
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uncommon	Tic-8	-	-
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SEQ 1 RRPXGXSXXR

RELATED SEQUENCES AVAILABLE WITH SEQLINK
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SR CA
LC STN Files: CA, CAPLUS, USPATFULL
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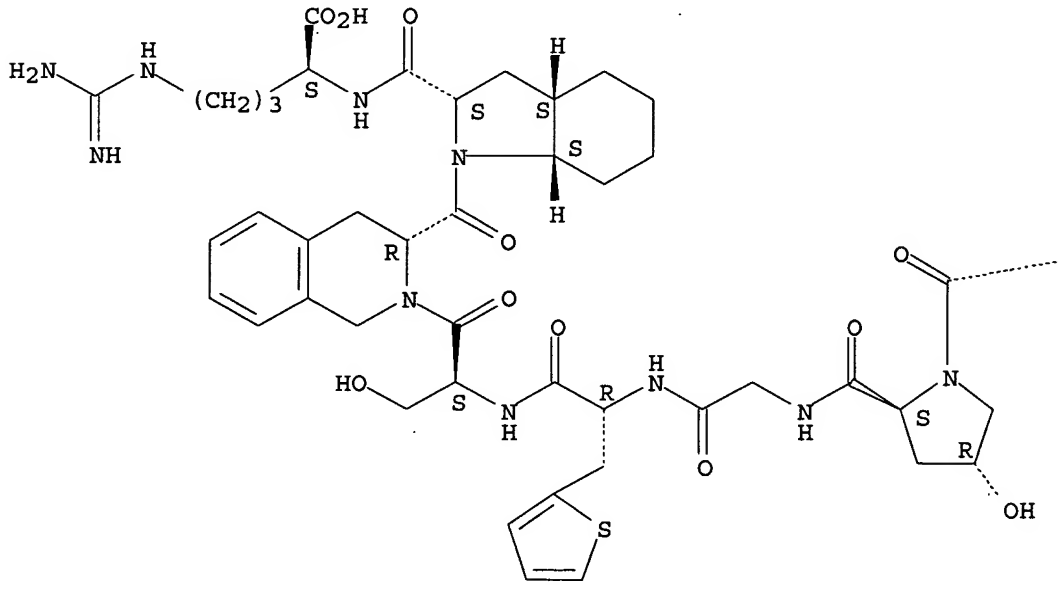
RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); USES (Uses)

Absolute stereochemistry.

PAGE 1-A



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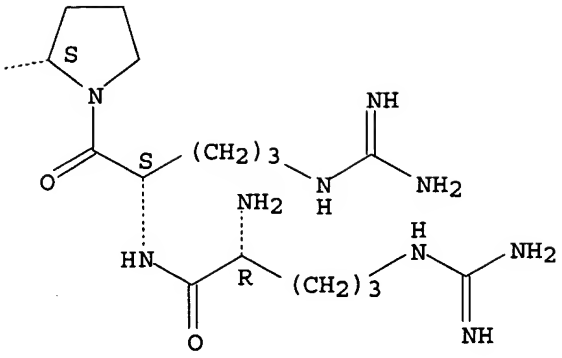

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1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 127:162123

L25 ANSWER 10 OF 23 REGISTRY COPYRIGHT 2005 ACS on STN
RN 193618-62-1 REGISTRY
CN D-Arginine, D-arginyl-L-arginyl-L-prolyl-(4R)-4-hydroxy-L-prolylglycyl-3-(2-thienyl)-L-alanyl-L-seryl-(3R)-1,2,3,4-tetrahydro-3-isoquinolinecarbonyl-(2S,3aS,7aS)-octahydro-1H-indole-2-carbonyl- (9CI) (CA INDEX NAME)
OTHER NAMES:
CN MEN 11646
FS PROTEIN SEQUENCE; STEREOSEARCH
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SEQ 1 RRPXGXSXXR

RELATED SEQUENCES AVAILABLE WITH SEQLINK
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LC STN Files: CA, CAPLUS, USPATFULL
DT.CA CAplus document type: Conference; Patent
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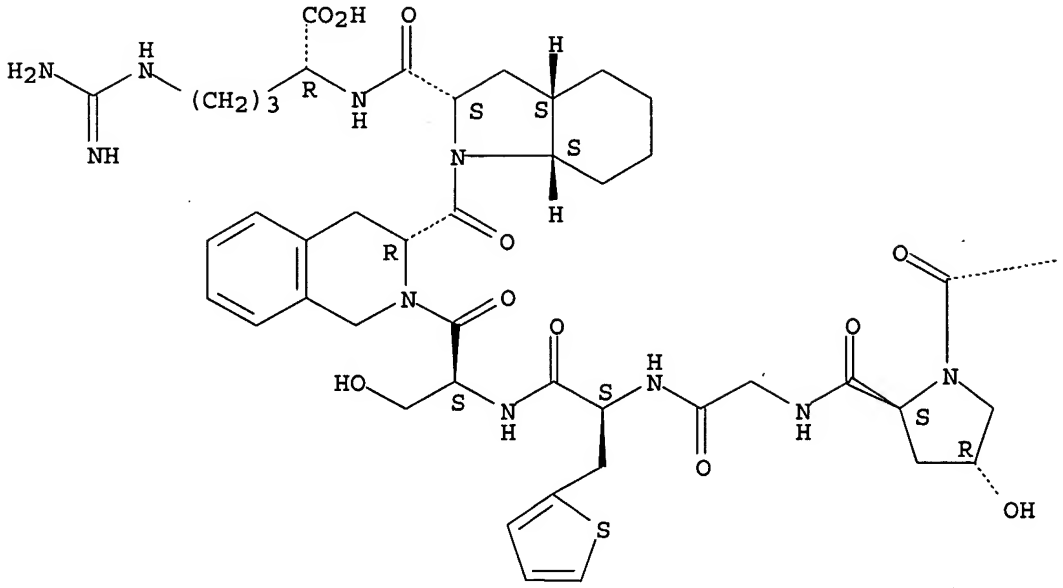
RL.NP Roles from non-patents: BIOL (Biological study); USES (Uses)

Absolute stereochemistry.

PAGE 1-A



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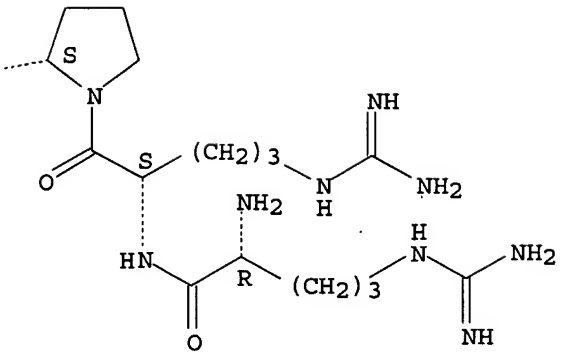

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REFERENCE 1: 141:151157

REFERENCE 2: 127:162123

L25 ANSWER 11 OF 23 REGISTRY COPYRIGHT 2005 ACS on STN

RN 193618-61-0 REGISTRY
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type	------ location ------		description
uncommon	Hyp-4	-	-
uncommon	Thi-6	-	-
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uncommon	Oic-9	-	-

SEQ 1 RRPXGXSXXR

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MF **C59 H89 N19 O13 S**
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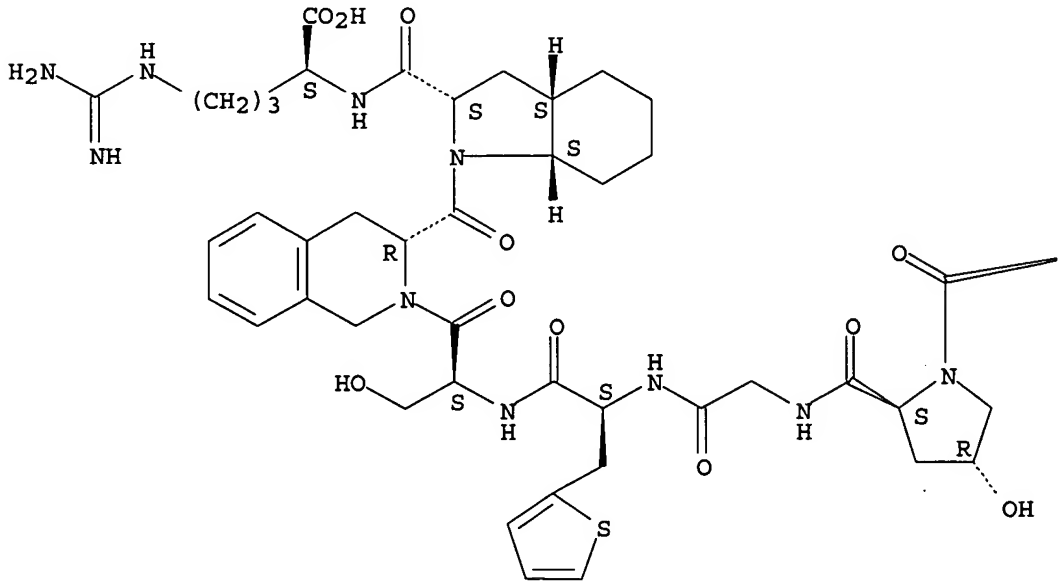
LC STN Files: CA, CAPLUS, USPATFULL
DT.CA CAplus document type: Patent
RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); USES (Uses)

Absolute stereochemistry.

PAGE 1-A



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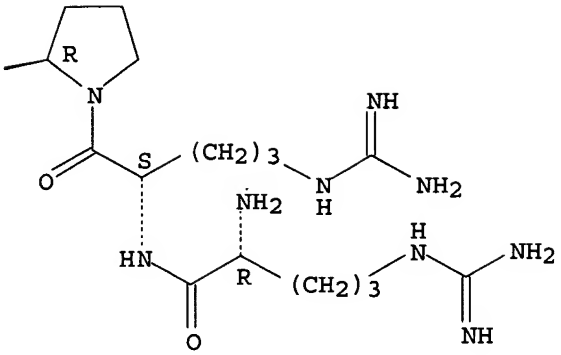

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 127:162123

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FS PROTEIN SEQUENCE; STEREOSEARCH
SQL **10**
NTE

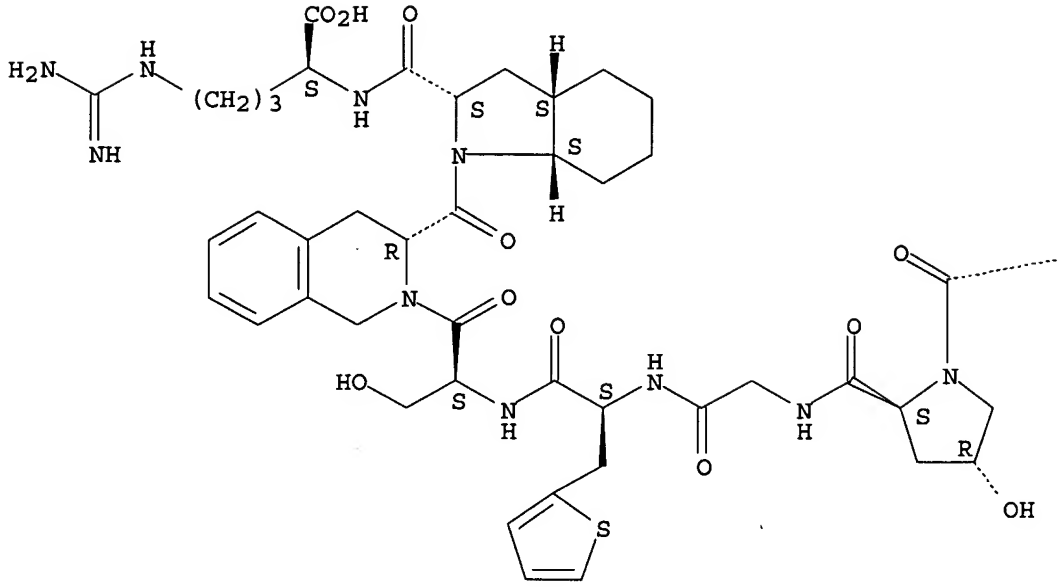
type	------ location ------		description
uncommon	Hyp-4	-	-
uncommon	Thi-6	-	-
uncommon	Tic-8	-	-
uncommon	Oic-9	-	-

SEQ 1 RRPXGXSXXR

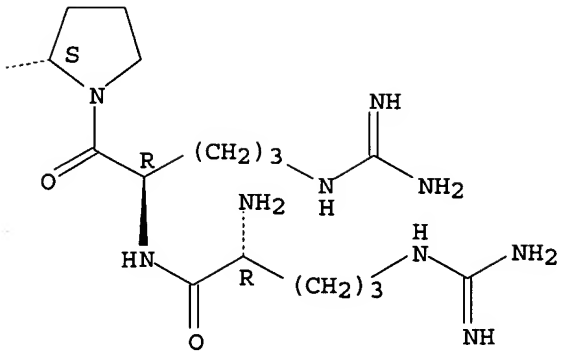
RELATED SEQUENCES AVAILABLE WITH SEQLINK
MF **C59 H89 N19 O13 S**
SR CA
LC STN Files: CA, CAPLUS, USPATFULL
DT.CA CAplus document type: Patent
RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); USES (Uses)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 127:162123

L25 ANSWER 13 OF 23 REGISTRY COPYRIGHT 2005 ACS on STN
RN 193618-59-6 REGISTRY
CN L-Arginine, L-arginyl-L-arginyl-L-prolyl-(4R)-4-hydroxy-L-prolylglycyl-3-(2-thienyl)-L-alanyl-L-seryl-(3R)-1,2,3,4-tetrahydro-3-

isoquinolinecarbonyl-(2S,3aS,7aS)-octahydro-1H-indole-2-carbonyl- (9CI)
(CA INDEX NAME)
FS PROTEIN SEQUENCE; STEREOSEARCH
SQL **10**
NTE

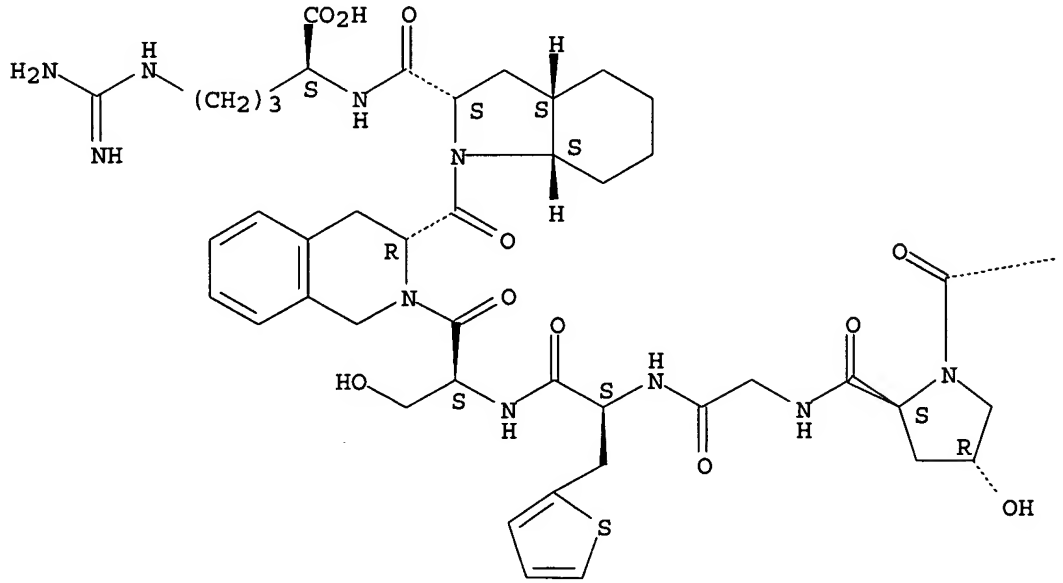
type	------ location ------		description
uncommon	Hyp-4	-	-
uncommon	Thi-6	-	-
uncommon	Tic-8	-	-
uncommon	Oic-9	-	-

SEQ 1 RRPXGXSXXR

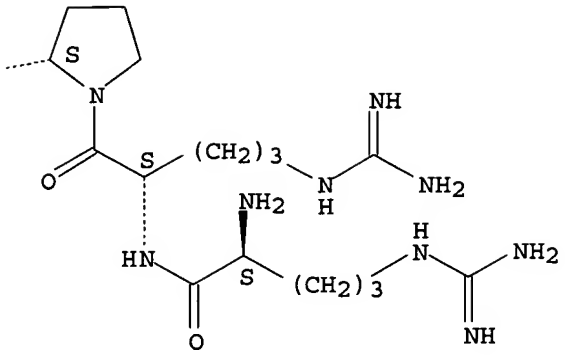
RELATED SEQUENCES AVAILABLE WITH SEQLINK
MF **C59 H89 N19 O13 S**
SR CA
LC STN Files: CA, CAPLUS, USPATFULL
DT.CA CAplus document type: Patent
RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); USES (Uses)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 127:162123

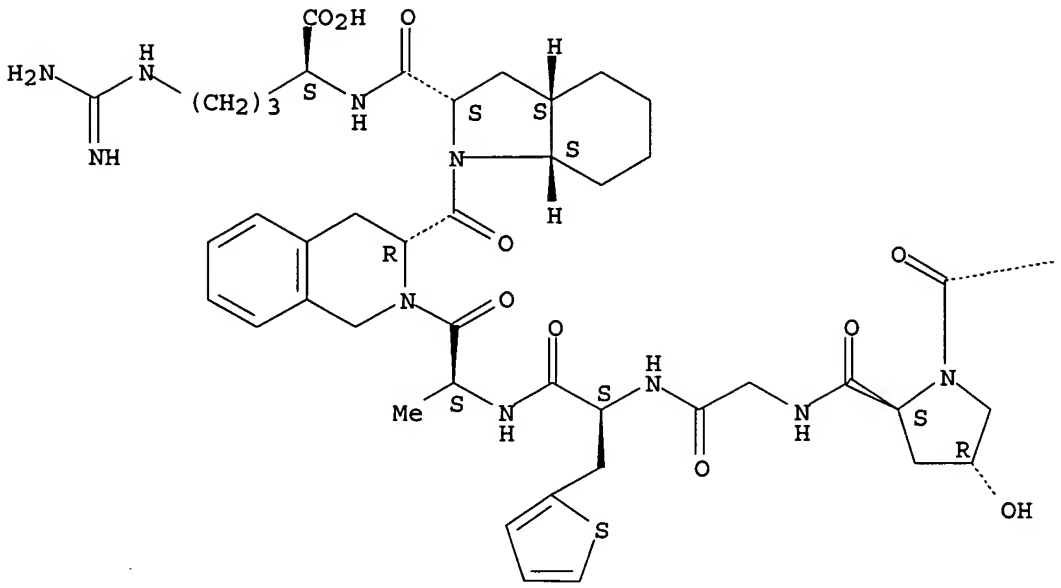
L25 ANSWER 14 OF 23 REGISTRY COPYRIGHT 2005 ACS on STN
RN 185145-94-2 REGISTRY
CN L-Arginine, D-arginyl-L-arginyl-L-prolyl-(4R)-4-hydroxy-L-prolylglycyl-3-(2-thienyl)-L-alanyl-L-alanyl-(3R)-1,2,3,4-tetrahydro-3-isoquinolinecarbonyl-(2S,3aS,7aS)-octahydro-1H-indole-2-carbonyl- (9CI) (CA INDEX NAME)
FS PROTEIN SEQUENCE; STEREOSEARCH
SQL **10**
NTE

type	------ location ------		description
uncommon	Hyp-4	-	-
uncommon	Thi-6	-	-
uncommon	Tic-8	-	-
uncommon	Oic-9	-	-

SEQ 1 RRPXGXAXXR
MF **C59 H89 N19 O12 S**
SR CA
LC STN Files: CA, CAPLUS, CASREACT
DT.CA CAplus document type: Journal
RL.NP Roles from non-patents: BIOL (Biological study); PREP (Preparation); PROC (Process); PRP (Properties)

Absolute stereochemistry.

PAGE 1-A



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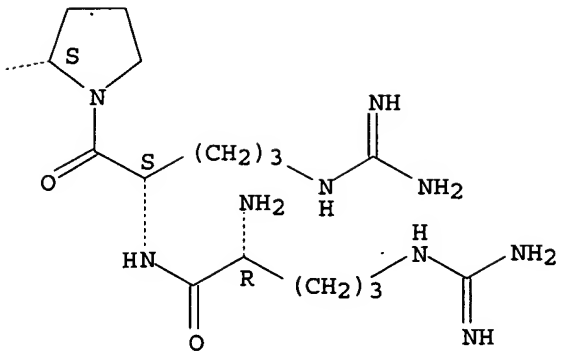


2 REFERENCES IN FILE CA (1907 TO DATE)
2 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 134:163320

REFERENCE 2: 126:54996

L25 ANSWER 15 OF 23 REGISTRY COPYRIGHT 2005 ACS on STN
RN 153322-84-0 REGISTRY

CN L-Arginine, D-arginyl-L-arginyl-L-prolyl-trans-4-hydroxy-L-prolylglycyl-3-(2-thienyl)-L-alanyl-L-seryl-L-1,2,3,4-tetrahydro-3-isoquinolinecarbonyl-L-(2α,3aβ,7aβ)-octahydro-1H-indole-2-carbonyl- (9CI) (CA INDEX NAME)
OTHER NAMES:
CN Win 65365
CN [L-Tic7]HOE-140
FS PROTEIN SEQUENCE; STEREOSEARCH
SQL **10**
NTE

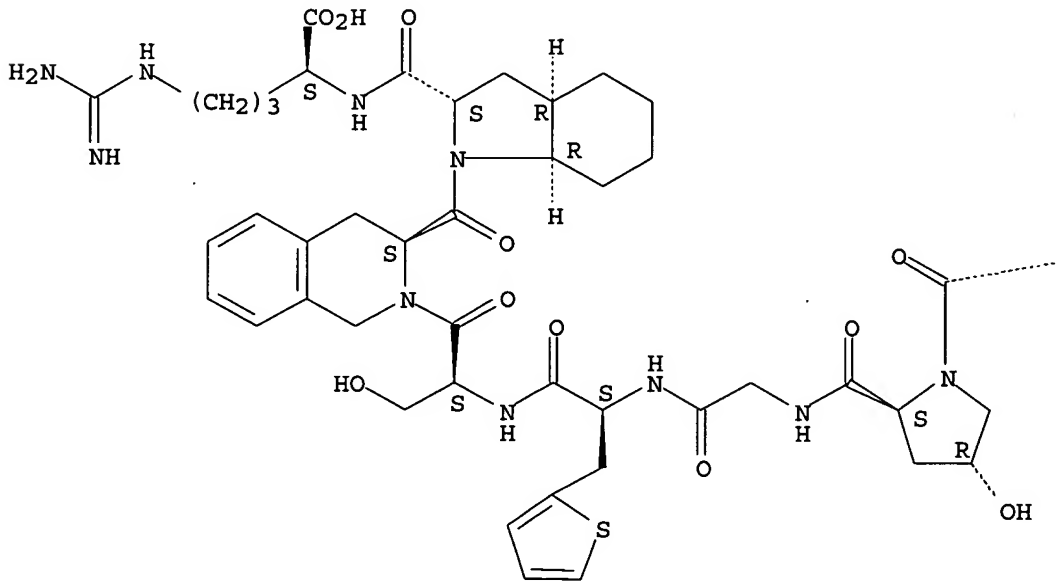
type	------ location ------		description
uncommon	Hyp-4	-	-
uncommon	Thi-6	-	-
uncommon	Tic-8	-	-
uncommon	Oic-9	-	-

SEQ 1 RRPXGXSXXR

RELATED SEQUENCES AVAILABLE WITH SEQLINK
MF **C59 H89 N19 O13 S**
SR CA
LC STN Files: CA, CAPLUS
DT.CA CAplus document type: Journal
RL.NP Roles from non-patents: BIOL (Biological study); PREP (Preparation); PRP (Properties)

Absolute stereochemistry.

PAGE 1-A



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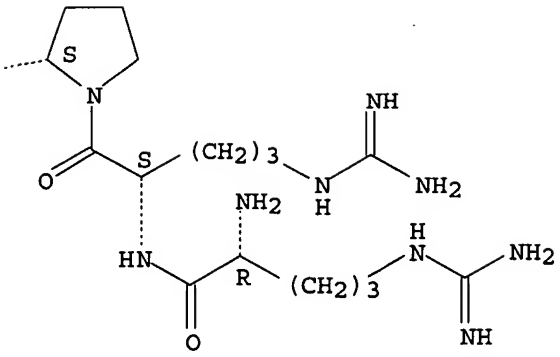


2 REFERENCES IN FILE CA (1907 TO DATE)
2 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 121:50783

REFERENCE 2: 120:153920

L25 ANSWER 16 OF 23 REGISTRY COPYRIGHT 2005 ACS on STN
RN 151009-41-5 REGISTRY
CN L-Arginine, D-arginyl-L-arginyl-L-prolyl-trans-4-hydroxy-L-prolylglycyl-3-(3-thienyl)-L-alanyl-L-seryl-D-1,2,3,4-tetrahydro-3-isoquinolinecarbonyl-L-octahydro-1H-indole-2-carbonyl- (9CI) (CA INDEX NAME)
OTHER NAMES:
CN Woe 1114-108A
FS PROTEIN SEQUENCE; STEREOSEARCH
SQL **10**
NTE

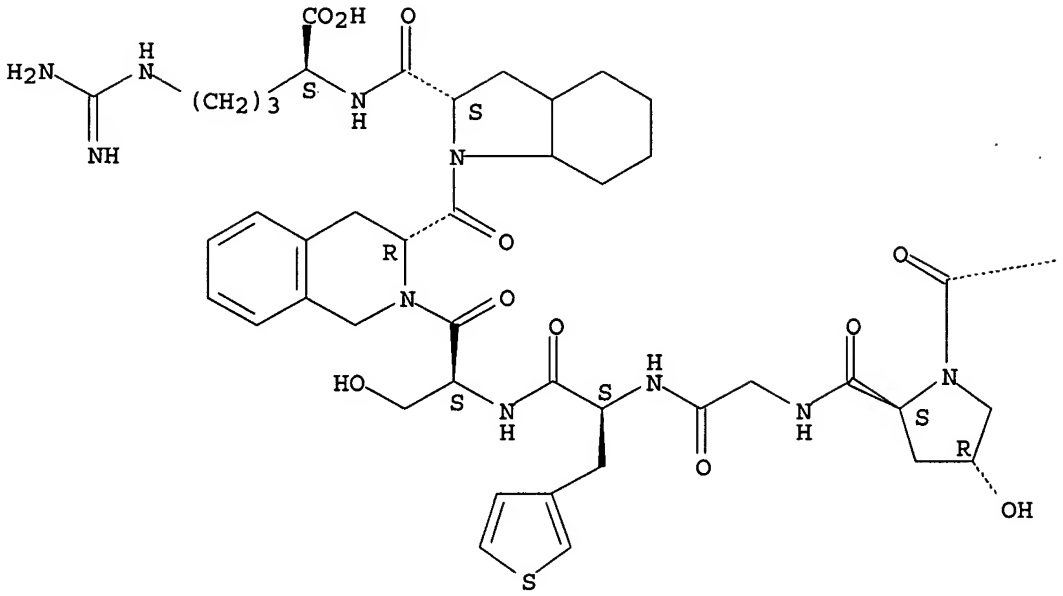
type	------ location ------		description
uncommon	Hyp-4	-	-
uncommon	Aaa-6	-	-
uncommon	Tic-8	-	-
uncommon	Oic-9	-	-
stereo	Arg-1	-	D
stereo	Tic-8	-	D

SEQ 1 RRPXGXSXXR

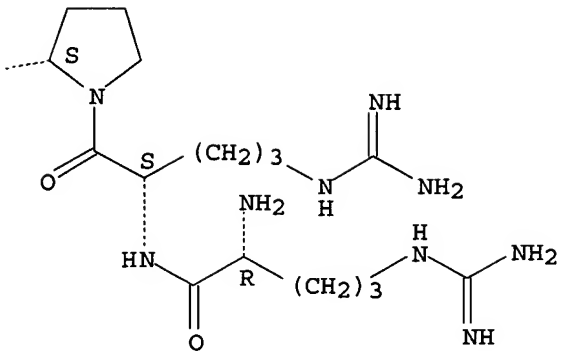
RELATED SEQUENCES AVAILABLE WITH SEQLINK
MF **C59 H89 N19 O13 S**
SR CA
LC STN Files: CA, CAPLUS
DT.CA CAplus document type: Conference
RL.NP Roles from non-patents: PROC (Process)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 119:220793

L25 ANSWER 17 OF 23 REGISTRY COPYRIGHT 2005 ACS on STN

RN 133162-76-2 REGISTRY
CN Bradykinin, N2-D-arginyl-3-(trans-4-hydroxy-L-proline)-7-(D-1,2,3,4-tetrahydro-3-isoquinolinecarboxylic acid)-8-[L-(2α,3aα,7aβ)-octahydro-1H-indole-2-carboxylic acid]-(9CI) (CA INDEX NAME)
FS PROTEIN SEQUENCE; STEREOSEARCH
SQL **10**
NTE

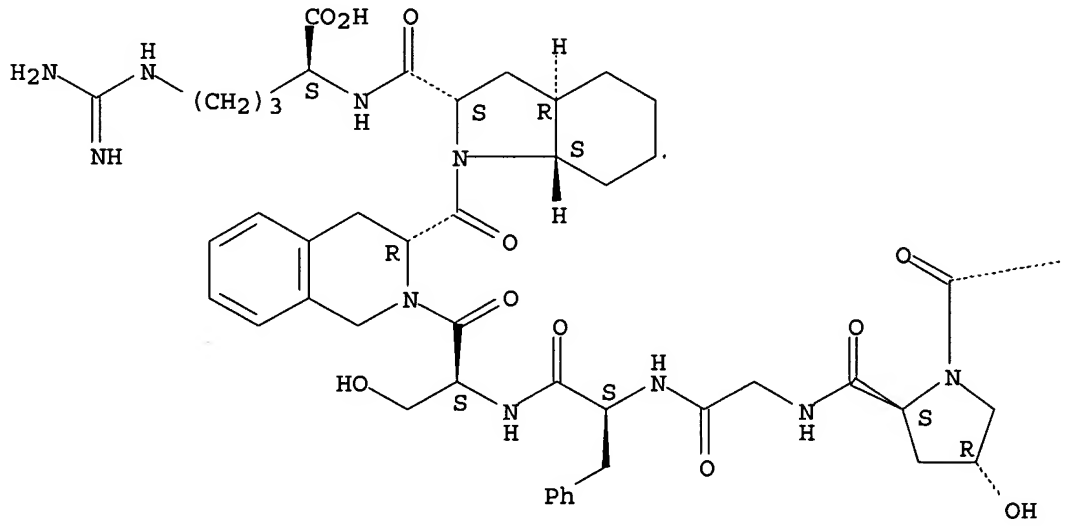
type	location		description
uncommon	Hyp-4	-	-
uncommon	Tic-8	-	-
uncommon	Oic-9	-	-

SEQ 1 RRPXGFSXXR

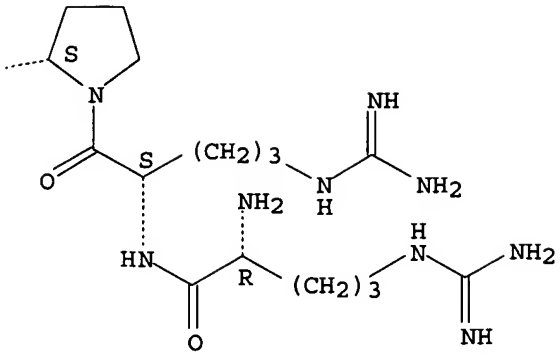
RELATED SEQUENCES AVAILABLE WITH SEQLINK
MF **C61 H91 N19 O13**
SR CA
LC STN Files: CA, CAPLUS
DT.CA CAplus document type: Journal
RL.NP Roles from non-patents: BIOL (Biological study)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 114:157636

L25 ANSWER 18 OF 23 REGISTRY COPYRIGHT 2005 ACS on STN
RN 133162-75-1 REGISTRY
CN L-Arginine, D-arginyl-L-arginyl-L-prolyl-(4R)-4-hydroxy-L-prolylglycyl-3-(2-thienyl)-L-alanyl-L-seryl-(3R)-1,2,3,4-tetrahydro-3-isoquinolinecarbonyl-(2S,3aR,7aS)-octahydro-1H-indole-2-carbonyl- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN L-Arginine, D-arginyl-L-arginyl-L-prolyl-trans-4-hydroxy-L-prolylglycyl-3-(2-thienyl)-L-alanyl-L-seryl-D-1,2,3,4-tetrahydro-3-isoquinolinecarbonyl-L-(2α,3aα,7aβ)-octahydro-1H-indole-2-carbonyl-
FS PROTEIN SEQUENCE; STEREOSEARCH
SQL **10**
NTE

type	location		description
uncommon	Hyp-4	-	-
uncommon	Thi-6	-	-
uncommon	Tic-8	-	-
uncommon	Oic-9	-	-

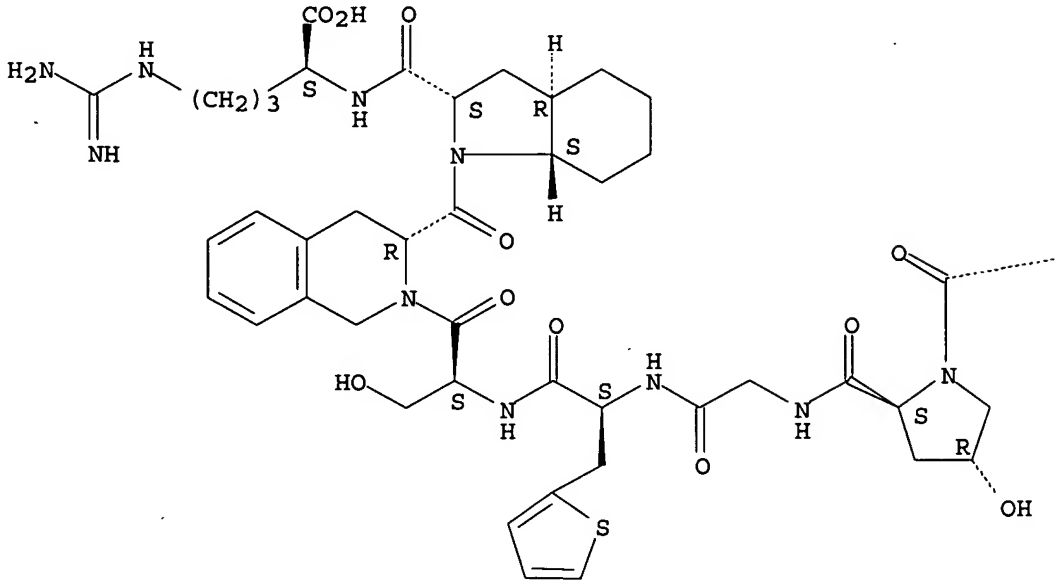
SEQ 1 RRPXGXSXXR

RELATED SEQUENCES AVAILABLE WITH SEQLINK
MF **C59 H89 N19 O13 S**
SR CA
LC STN Files: CA, CAPLUS, USPATFULL
DT.CA CAplus document type: Journal; Patent
RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); USES (Uses)

RL.NP Roles from non-patents: BIOL (Biological study)

Absolute stereochemistry.

PAGE 1-A



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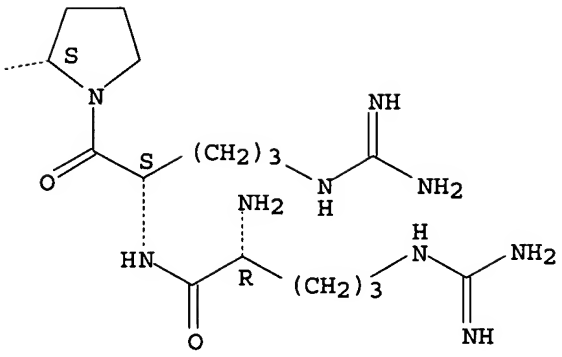


2 REFERENCES IN FILE CA (1907 TO DATE)
2 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 127:162123

REFERENCE 2: 114:157636

L25 ANSWER 19 OF 23 REGISTRY COPYRIGHT 2005 ACS on STN
RN 130404-96-5 REGISTRY
CN L-Arginine, D-arginyl-L-arginyl-L-prolyl-(4R)-4-hydroxy-L-prolylglycyl-3-(2-thienyl)-L-alanyl-L-seryl-(3R)-1,2,3,4-tetrahydro-3-isoquinolinecarbonyl-(2R,3aR,7aR)-octahydro-1H-indole-2-carbonyl- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN L-Arginine, D-arginyl-L-arginyl-L-prolyl-trans-4-hydroxy-L-prolylglycyl-3-(2-thienyl)-L-alanyl-L-seryl-D-1,2,3,4-tetrahydro-3-isoquinolinecarbonyl-D-(2α,3aβ,7aβ)-octahydro-1H-indole-2-carbonyl-
FS PROTEIN SEQUENCE; STEREOSEARCH
SQL **10**
NTE

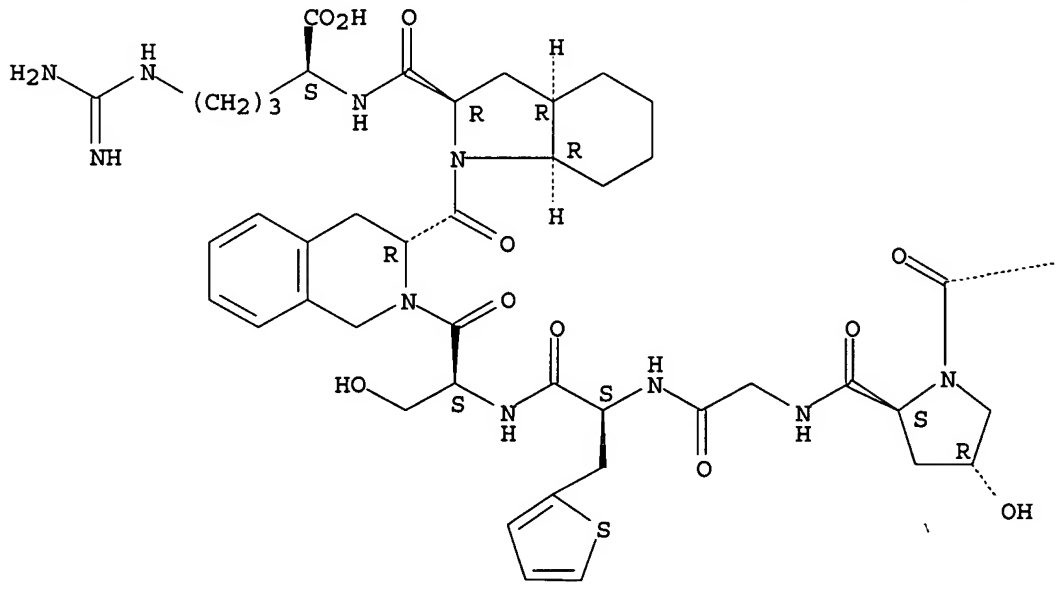
type	------ location ------		description
uncommon	Hyp-4	-	-
uncommon	Thi-6	-	-
uncommon	Tic-8	-	-
uncommon	Oic-9	-	-

SEQ 1 RRPXGXSXXR

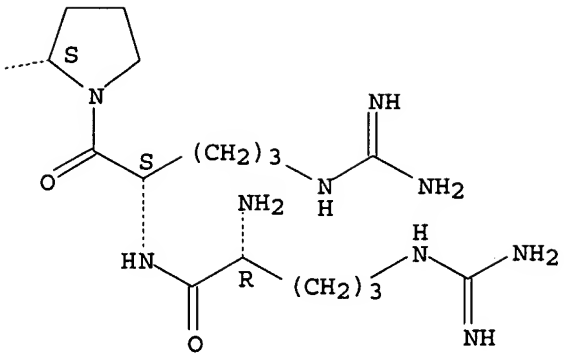
RELATED SEQUENCES AVAILABLE WITH SEQLINK
MF **C59 H89 N19 O13 S**
SR CA
LC STN Files: CA, CAPLUS, USPATFULL
DT.CA CAplus document type: Patent
RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); USES (Uses)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



2 REFERENCES IN FILE CA (1907 TO DATE)
2 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 127:162123

REFERENCE 2: 114:207831

L25 ANSWER 20 OF 23 REGISTRY COPYRIGHT 2005 ACS on STN
RN 130334-55-3 REGISTRY
CN Bradykinin, N2-D-arginyl-3-(trans-4-hydroxy-L-proline)-7-(D-1,2,3,4-tetrahydro-3-isoquinolinecarboxylic acid)-8-[L-(2α,3aβ,7aβ)-octahydro-1H-indole-2-carboxylic acid]- (9CI) (CA INDEX NAME)
OTHER NAMES:
CN NPC 18545
FS PROTEIN SEQUENCE; STEREOSEARCH
SQL **10**
NTE

type	location		description
uncommon	Hyp-4	-	-
uncommon	Tic-8	-	-
uncommon	Oic-9	-	-

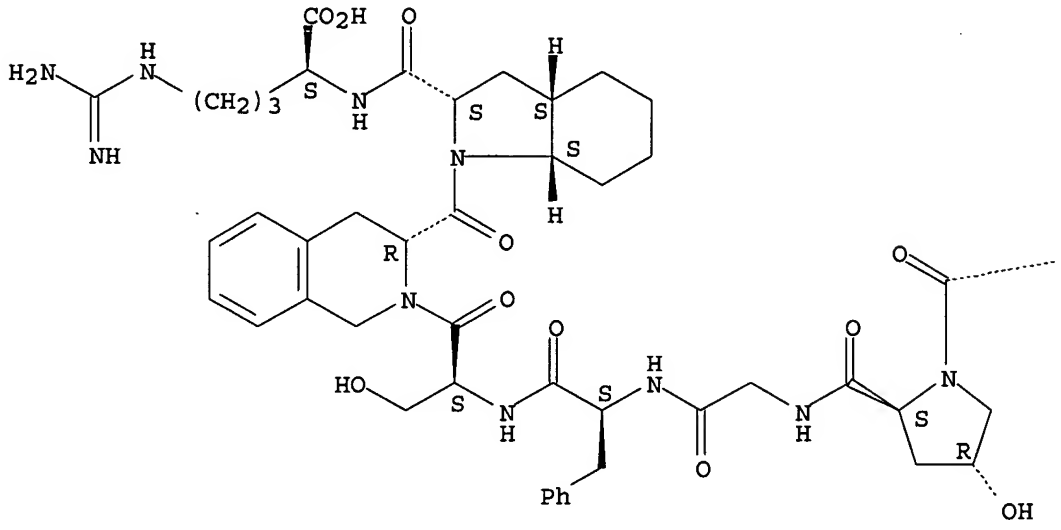
SEQ 1 RRPXGFSXXR

RELATED SEQUENCES AVAILABLE WITH SEQLINK
MF **C61 H91 N19 O13**
SR CA
LC STN Files: BIOSIS, CA, CAPLUS, PHAR, TOXCENTER, USPATFULL
DT.CA CAplus document type: Conference; Journal; Patent
RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); USES (Uses)

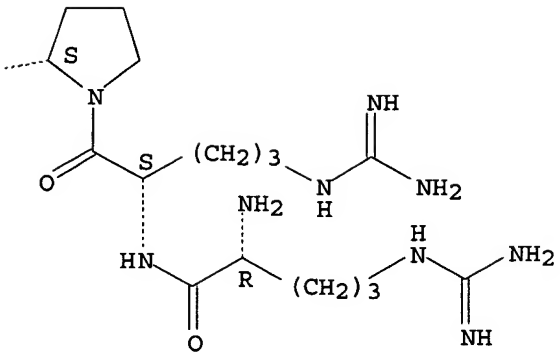
RL.NP Roles from non-patents: BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



11 REFERENCES IN FILE CA (1907 TO DATE)
11 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 128:290242

REFERENCE 2: 127:314823

REFERENCE 3: 127:162123

REFERENCE 4: 121:281159

REFERENCE 5: 120:290682

REFERENCE 6: 120:208607

REFERENCE 7: 119:250452

REFERENCE 8: 119:41697

REFERENCE 9: 118:261015

REFERENCE 10: 116:188596

L25 ANSWER 21 OF 23 REGISTRY COPYRIGHT 2005 ACS on STN
RN 130308-53-1 REGISTRY
CN Bradykinin, N2-D-arginyl-7-(D-1,2,3,4-tetrahydro-3-isoquinolinecarboxylic acid)-8-[(2α,3aβ,7aβ)-L-octahydro-1H-indole-2-carboxylic acid]- (9CI) (CA INDEX NAME)
FS PROTEIN SEQUENCE; STEREOSEARCH
SQL **10**
NTE

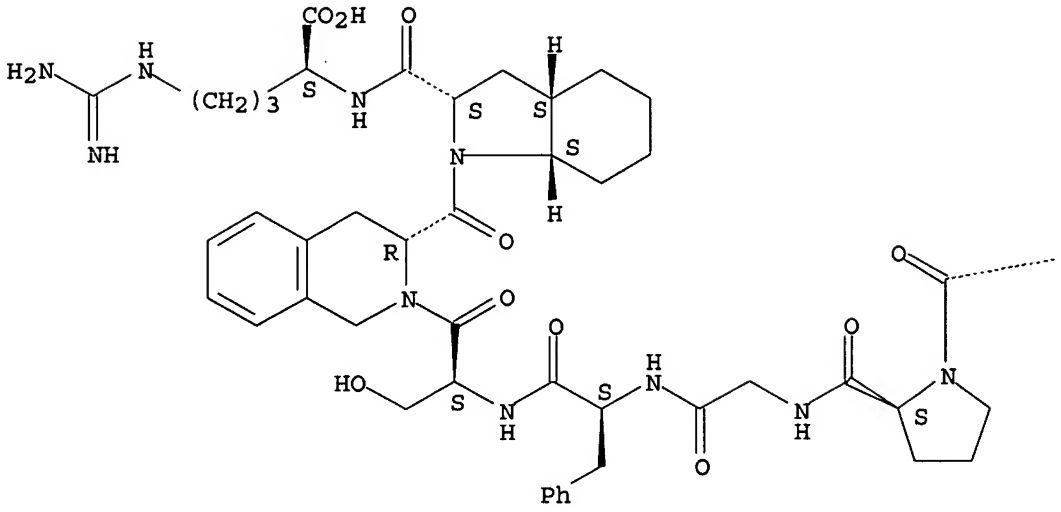
type	------ location ------		description
uncommon	Tic-8	-	-
uncommon	Oic-9	-	-

SEQ 1 RRPPGFSXXR

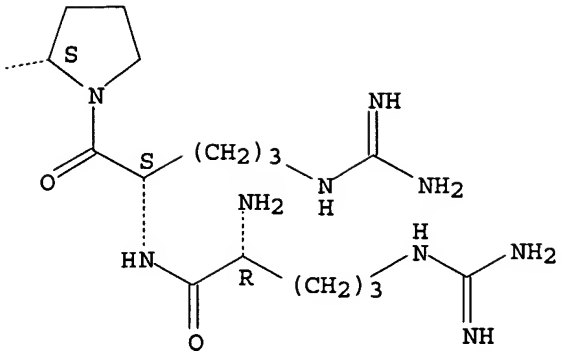
RELATED SEQUENCES AVAILABLE WITH SEQLINK
MF **C61 H91 N19 O12**
SR CA
LC STN Files: CA, CAPLUS, USPATFULL
DT.CA CAplus document type: Journal; Patent
RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); USES (Uses)
RLD.NP Roles for non-specific derivatives from non-patents: BIOL (Biological study); PREP (Preparation)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



3 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
3 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 127:162123

REFERENCE 2: 125:168616

REFERENCE 3: 114:207831

L25 ANSWER 22 OF 23 REGISTRY COPYRIGHT 2005 ACS on STN
RN 130308-52-0 REGISTRY

CN Bradykinin, N2-D-arginyl-2-(trans-4-hydroxy-L-proline)-7-(D-1,2,3,4-tetrahydro-3-isoquinolinecarboxylic acid)-8-[(2α,3aβ,7aβ)-L-octahydro-1H-indole-2-carboxylic acid]- (9CI) (CA INDEX NAME)
FS PROTEIN SEQUENCE; STEREOSEARCH
SQL **10**
NTE

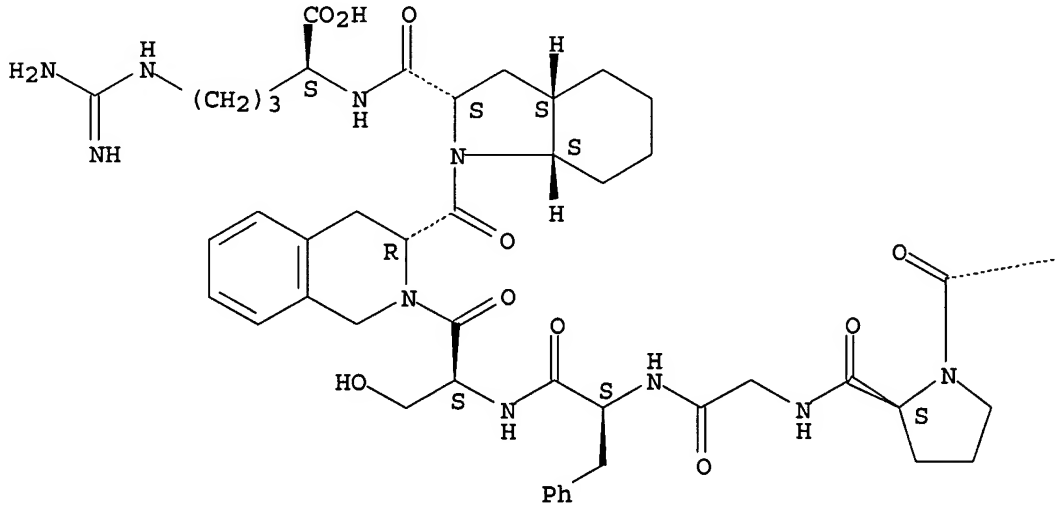
type	------ location ------		description
uncommon	Hyp-3	-	-
uncommon	Tic-8	-	-
uncommon	Oic-9	-	-

SEQ 1 RRXPGFSXXR

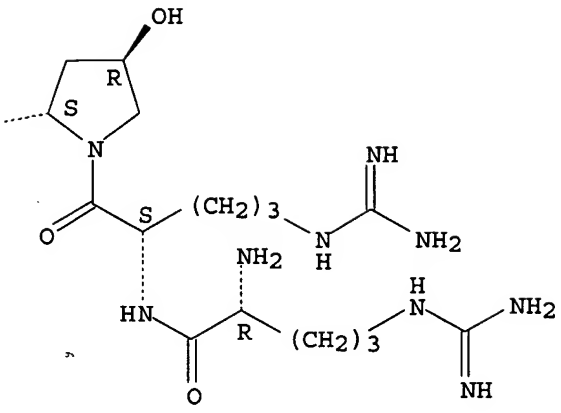
RELATED SEQUENCES AVAILABLE WITH SEQLINK
MF **C61 H91 N19 O13**
SR CA
LC STN Files: CA, CAPLUS, USPATFULL
DT.CA CAplus document type: Patent
RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); USES (Uses)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



2 REFERENCES IN FILE CA (1907 TO DATE)
2 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 127:162123

REFERENCE 2: 114:207831

L25 ANSWER 23 OF 23 REGISTRY COPYRIGHT 2005 ACS on STN
RN **130308-49-5** REGISTRY
CN L-Arginine, D-arginyl-L-arginyl-L-prolyl-L-prolylglycyl-3-(2-thienyl)-L-alanyl-L-seryl-(3R)-1,2,3,4-tetrahydro-3-isoquinolinecarbonyl-(2S,3aS,7aS)-octahydro-1H-indole-2-carbonyl- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Bradykinin, N2-D-arginyl-5-[3-(2-thienyl)-L-alanine]-7-(D-1,2,3,4-tetrahydro-3-isoquinolinecarboxylic acid)-8-[(2α,3aβ,7aβ)-L-octahydro-1H-indole-2-carboxylic acid]-
FS PROTEIN SEQUENCE; STEREOSEARCH
SQL **10**
NTE

type	location		description
uncommon	Thi-6	-	-
uncommon	Tic-8	-	-
uncommon	Oic-9	-	-

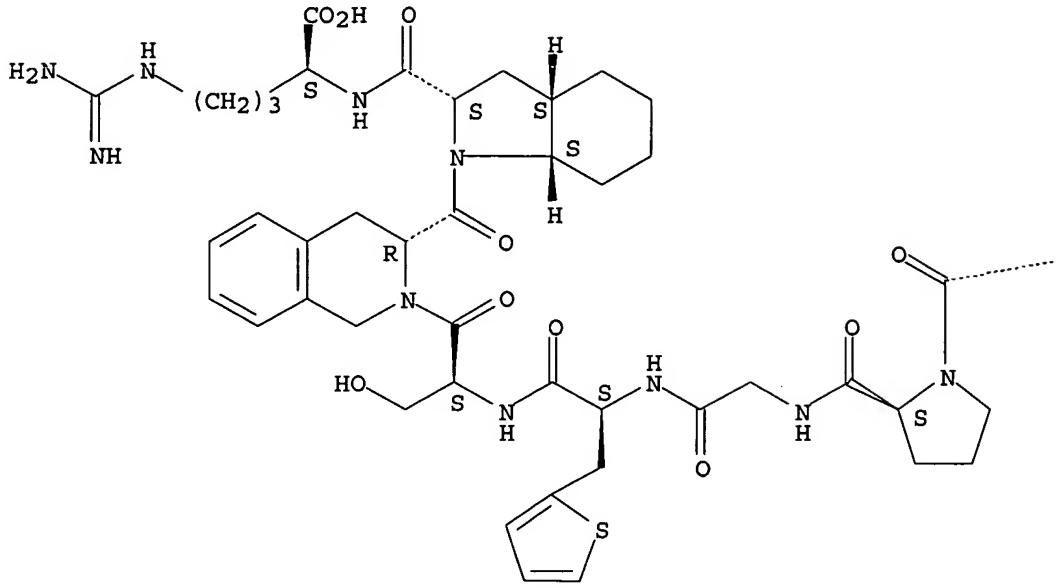
SEQ 1 RRPPGXSXXR

RELATED SEQUENCES AVAILABLE WITH SEQLINK
DR 197370-25-5
MF C59 H89 N19 O12 S
SR CA
LC STN Files: CA, CAPLUS, USPATFULL
DT.CA CAplus document type: Patent
RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); PRP

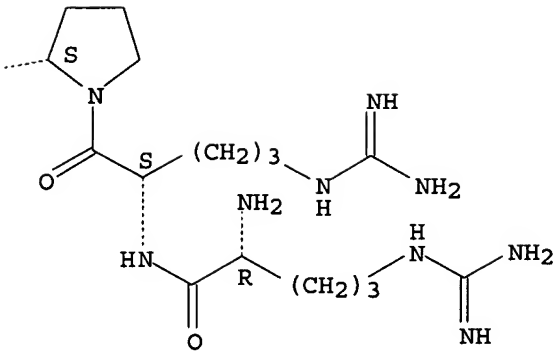
(Properties); USES (Uses)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



7 REFERENCES IN FILE CA (1907 TO DATE)
7 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 141:185137

REFERENCE 2: 128:290242

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REFERENCE   3:  127:314823

REFERENCE   4:  127:162123

REFERENCE   5:  120:208607

REFERENCE   6:  118:261015

REFERENCE   7:  114:207831


=> d his

     (FILE 'HOME' ENTERED AT 07:06:50 ON 27 SEP 2005)
               SET COST OFF

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L1             1 S US20040248809/PN OR (US2004-773772# OR US2003-480246# OR DE20
               E MICHAELIS/AU
L2             5 S E3
               E MICHAELIS M/AU
L3           133 S E3-E5,E9-E11
               E RUDOLPHI/AU
L4            93 S E3,E13-E17
               E AVENTI/PA,CS
L5          2556 S AVENTIS?/PA,CS
               SEL RN L1

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L6             7 S E1-E7
L7             6 S L6 AND SQL/FA
               E C61H91N19O12/MF
L8             2 S E3 AND SQL/FA
               E C61H91N19O13/MF
L9            10 S E3 AND SQL/FA
               E C59H89N19O12S/MF
L10            3 S E3 AND SQL/FA
               E C59H89N19O13S/MF
L11           14 S E3 AND SQL/FA
L12           23 S L8-L11 NOT L7
L13           18 S L12 NOT (ASPARAG? OR CYCLOPENT? OR LEUC?)
L14           24 S L7,L13
               SAV L14 GARCIA773/A
               SEL RN
L15            1 S E1-E24/CRN
L16           74 SEQLINK EXACT L14
L17           49 S L16 NOT L14,L15

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L18            0 S L14 OR L15

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L19          319 S L14 OR L15
L20            7 S L7
L21            4 S L2-L5 AND L19
L22            2 S L2-L5 AND L20
L23            4 S L21,L22
L24            9 S L20-L23,L1
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L25           23 S L14 NOT 130308-48-4

     FILE 'HCAPLUS' ENTERED AT 07:29:17 ON 27 SEP 2005
L26           21 S L25
L27            2 S L1-L5 AND L26
L28           21 S L26 AND (PD<=20030620 OR PRD<=20030620 OR AD<=20030620)
L29           21 S L26,L28

     FILE 'USPATFULL' ENTERED AT 07:30:19 ON 27 SEP 2005
L30            6 S L25

     FILE 'REGISTRY' ENTERED AT 07:31:18 ON 27 SEP 2005

=> fil uspatful
FILE 'USPATFULL' ENTERED AT 07:31:39 ON 27 SEP 2005
CA INDEXING COPYRIGHT (C) 2005 AMERICAN CHEMICAL SOCIETY (ACS)

FILE COVERS 1971 TO PATENT PUBLICATION DATE: 22 Sep 2005 (20050922/PD)
FILE LAST UPDATED: 22 Sep 2005 (20050922/ED)
HIGHEST GRANTED PATENT NUMBER: US6948186
HIGHEST APPLICATION PUBLICATION NUMBER: US2005210555
CA INDEXING IS CURRENT THROUGH 22 Sep 2005 (20050922/UPCA)
ISSUE CLASS FIELDS (/INCL) CURRENT THROUGH: 22 Sep 2005 (20050922/PD)
REVISED CLASS FIELDS (/NCL) LAST RELOADED: Aug 2005
USPTO MANUAL OF CLASSIFICATIONS THESAURUS ISSUE DATE: Aug 2005

>>>  USPAT2 is now available.  USPATFULL contains full text of the     <<<
>>>  original, i.e., the earliest published granted patents or         <<<
>>>  applications.  USPAT2 contains full text of the latest US         <<<
>>>  publications, starting in 2001, for the inventions covered in     <<<
>>>  USPATFULL.  A USPATFULL record contains not only the original     <<<
>>>  published document but also a list of any subsequent              <<<
>>>  publications.  The publication number, patent kind code, and      <<<
>>>  publication date for all the US publications for an invention     <<<
>>>  are displayed in the PI (Patent Information) field of USPATFULL   <<<
>>>  records and may be searched in standard search fields, e.g., /PN, <<<
>>>  /PK, etc.                                                         <<<

>>>  USPATFULL and USPAT2 can be accessed and searched together         <<<
>>>  through the new cluster USPATALL.  Type FILE USPATALL to          <<<
>>>  enter this cluster.                                               <<<
>>>                                                                    <<<
>>>  Use USPATALL when searching terms such as patent assignees,       <<<
>>>  classifications, or claims, that may potentially change from      <<<
>>>  the earliest to the latest publication.                           <<<

This file contains CAS Registry Numbers for easy and accurate
substance identification.

=> d l30 bib abs hitrn tot

L30  ANSWER 1 OF 6  USPATFULL on STN
AN     2004:315133  USPATFULL
TI     Use of antagonists of the bradykinin B2 receptor for the treatment of
       osteoarthrosis
IN     Michaelis, Martin, Frankfurt, GERMANY, FEDERAL REPUBLIC OF
       Rudolphi, Karl, Mainz, GERMANY, FEDERAL REPUBLIC OF
PA     Aventis Pharma Deutschland GmbH, Frankfurt am Main, GERMANY, FEDERAL
       REPUBLIC OF (non-U.S. corporation)
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PI US 2004248809 A1 20041209
AI US 2004-773772 A1 20040206 (10)
PRAI DE 2003-10304994 20030207
US 2003-480246P 20030620 (60)
DT Utility
FS APPLICATION
LREP ROSS J. OEHLER, AVENTIS PHARMACEUTICALS INC., ROUTE 202-206, MAIL CODE: D303A, BRIDGEWATER, NJ, 08807
CLMN Number of Claims: 7
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 614
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Peptides having bradykinin-antagonistic action are suitable for the production of pharmaceuticals for the prophylaxis and therapy of diseases in whose course an increased activity of matrix metalloproteinases is involved. These include diseases such as degenerative joint diseases, for example osteoarthrosis, spondylosis and chondroporosis after joint trauma or relatively long immobilization of a joint after meniscus or patella injuries or torn ligaments. The invention therefore relates to the use of a compound of the formula I,

A-B-X-E-F-K-(D)-TIC-G-M-F'-I (I)

for the production of pharmaceuticals for the treatment of degenerative joint diseases, wherein A, B, X, E, F, K, (D)-TIC, G, M, F' and I are as defined herein.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IT **130308-49-5 199870-83-2 740808-61-1 740808-62-2 740808-63-3 740808-64-4**
(bradykinin B2 receptor antagonists for treating osteoarthritis and other matrix metalloproteinase-associated diseases)

L30 ANSWER 2 OF 6 USPATFULL on STN
AN 2003:251632 USPATFULL
TI PROKINETIC AGENTS FOR TREATING GASTRIC HYPOMOTILITY AND RELATED DISORDERS
IN WATSON, JOHN W., LEDYARD, CT, UNITED STATES
ANDREWS, PAUL L. R., LONDON, UNITED KINGDOM
WOODS, ANTHONY J., LONDON, UNITED KINGDOM
PI US 2003176421 A1 20030918
AI US 1999-476253 A1 19991230 (9)
DT Utility
FS APPLICATION
LREP PFIZER INC, 150 EAST 42ND STREET, 5TH FLOOR - STOP 49, NEW YORK, NY, 10017-5612
CLMN Number of Claims: 41
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 4249
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Stasis is treated or prevented in all or any part or parts of the stomach of a patient, especially a human patient, in need of such treatment, where said stasis results from hypomotility in the stomach, particularly gastric hypomotility with delayed emptying of the liquid and/or solid contents of the stomach. Gastric or gastrointestinal disorders are also treated which are characterized by one or more symptoms selected from pain, nausea, vomiting, heartburn, postprandial discomfort, indigestion and gastroesophageal reflux. Such treatment or

prevention is achieved by administering to the patient a therapeutically effective amount of an inhibitor of phosphodiesterase-4 (PDE4), including isozyme subtypes thereof, sufficient to treat or prevent such hypomotility or gastric or gastrointestinal disorder in said patient. The PDE4 inhibitor comprises a compound of Formula (IA) or (IB): ##STR1##

where in a preferred embodiment, R is cyclopentyl or cyclohexyl; R.sup.1 is (C.sub.1-C.sub.2) alkyl; one of R.sup.2.sub.a and R.sup.2.sub.b is hydrogen and the other is a substituent of partial Formula (1.0.0) above, where the dashed line represents a single bond, m is 0, R.sup.113 and R.sup.114 are in a cis relationship to each other, R.sup.113 is cyano, R.sup.115 is hydrogen, and R.sup.114 is carboxy, --CH.sub.2OH, or --CH.sub.2C(.dbd.O)NH.sub.2.

Pharmaceutical compositions are also described which are useful for carrying out the above-mentioned methods of treatment and prevention, and which are also useful in the treatment of a gastric or gastrointestinal disorder in a patient which comprises with respect to said patient, (i) a sign or concomitant of diabetic neuropathy, anorexia nervosa, achlorhydria, gastrointestinal surgery, post-surgical recovery in the period of emergence from general anesthesia; or the administration of morphine and morphine-like opioids; (ii) a secondary aspect of a primary disease or disorder in said patient which is organic, wherein said disease or disorder involves particularly a gastroenteric or gastroesophageal organ or tissue, or an organ or tissue of the central nervous system of said patient; or (iii) an adverse side effect of a different therapeutic agent administered to said patient in the course of treating another unrelated disease or disorder in said patient.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IT **603969-58-0**
(as auxiliary therapeutic agent; prokinetic phosphodiesterase-4 inhibitor agents for treating gastric hypomotility and related disorders)

L30 ANSWER 3 OF 6 USPATFULL on STN
AN 2001:86438 USPATFULL
TI Use of peptidic bradykinin antagonists for the treatment and prevention of Alzheimer's disease
IN Heitsch, Holger, Mainz-Kastel, Germany, Federal Republic of
Henke, Stephan, Hofheim, Germany, Federal Republic of
Breipohl, Gerhard, Frankfurt, Germany, Federal Republic of
Knolle, Jochen, Kriftel, Germany, Federal Republic of
Wirth, Klaus, Kriftel, Germany, Federal Republic of
Wiemer, Gabriele, Kronberg, Germany, Federal Republic of
PA Aventis Pharma Deutschland GmbH, Frankfurt am Main, Germany, Federal Republic of (non-U.S. corporation)
PI US 6245736 B1 20010612
AI US 1997-949496 19971014 (8)
PRAI DE 1996-19642289 19961014
DT Utility
FS GRANTED
EXNAM Primary Examiner: Jones, Dwayne C.; Assistant Examiner: Delacroix-Muirheid, C.
LREP Finnegan, Henderson, Farabow, Garrett and Dunner, L.L.P.
CLMN Number of Claims: 15
ECL Exemplary Claim: 1
DRWN No Drawings

LN.CNT 626
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The invention relates to the use of bradykinin antagonists for the production of pharmaceuticals for the treatment and prevention of Alzheimer's disease. Suitable bradykinin antagonists are peptides which inhibit the effects of the Alzheimer's protein amyloid (β/A4) on isolated endothelial cells. A particularly suitable peptide is H-D-Arg-Arg-Pro-Hyp-Gly-Thi-Ser-D-Tic-Oic-Arg-OH (HOE 140) and its physiologically tolerable salts.

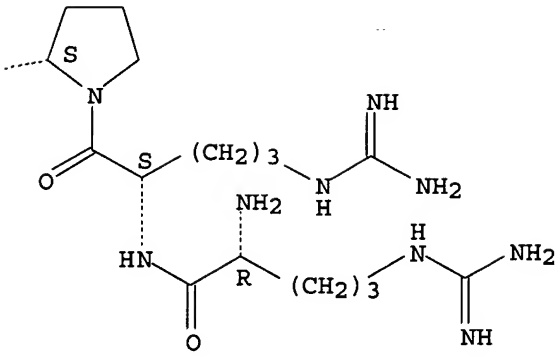
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IT **130308-49-5 130334-55-3**
(use of bradykinin antagonists for treatment and prevention of Alzheimer's disease)

L30 ANSWER 4 OF 6 USPATFULL on STN
AN 1999:12910 USPATFULL
TI Use of bradykinin antagonists for the production of pharmaceuticals for the treatment of chronic fibrogenetic liver disorders and acute liver disorders
IN Breipohl, Gerhard, Frankfurt, Germany, Federal Republic of
Henke, Stephan, Hofheim, Germany, Federal Republic of
Knolle, Jochen, Kriftel, Germany, Federal Republic of
Wirth, Klaus, Kriftel, Germany, Federal Republic of
Hropot, Max, Florsheim, Germany, Federal Republic of
Bickel, Martin, Bad Homburg, Germany, Federal Republic of
PA Hoechst Aktiengesellschaft, Frankfurt am Main, Germany, Federal Republic of (non-U.S. corporation)
PI US 5863901 19990126
AI US 1997-810012 19970304 (8)
PRAI DE 1996-19612067 19960327
DT Utility
FS Granted
EXNAM Primary Examiner: Tsang, Cecilia J.; Assistant Examiner: Delacroix-Muirheid, C.
LREP Finnegan, Henderson, Farabow, Garrett & Dunner, L.L.P.
CLMN Number of Claims: 16
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 1036
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB This invention relates to a method of treating a chronic fibrogenetic liver disorder and/or an acute liver disorder and/or complications associated therewith, comprising administering to a patient a therapeutically effective amount of a bradykinin antagonist. Particular complications associated with said liver disorders include portal hypertension, decompensation phenomena such as ascites, edema formation, hepatorenal syndrome, hypertensive gastropathy and colopathy, splenomegaly and hemorrhagic complications in the gastrointestinal tract due to portal hypertension, collateral circulation and hyperemia and a cardiopathy as a result of a chronically hyperdynamic circulatory situation and its consequences.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IT **130308-49-5 130334-55-3**
(use of bradykinin antagonists for treatment of chronic fibrogenic liver diseases)

L30 ANSWER 5 OF 6 USPATFULL on STN
AN 97:86726 USPATFULL

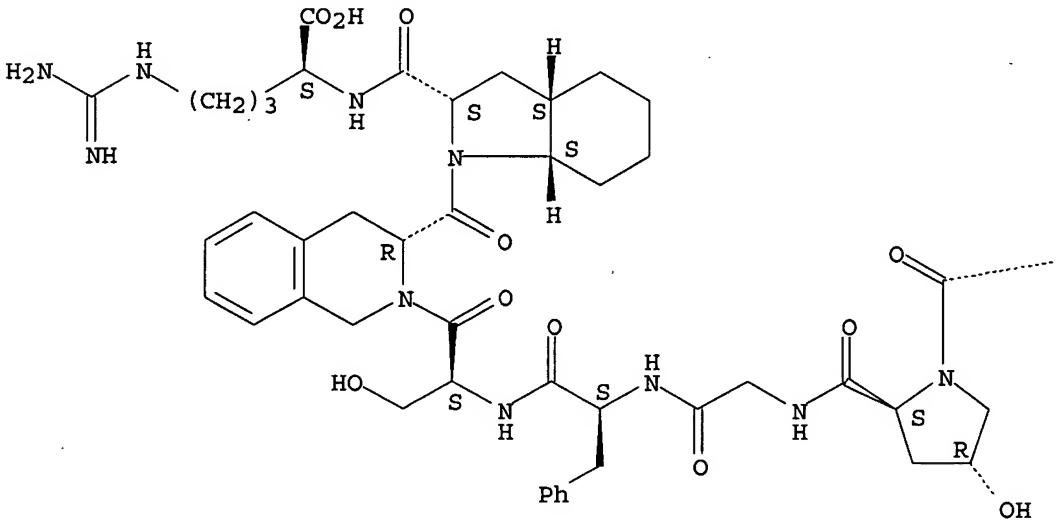
PAGE 1-B



RN 130334-55-3 HCAPLUS
CN Bradykinin, N2-D-arginyl-3-(trans-4-hydroxy-L-proline)-7-(D-1,2,3,4-tetrahydro-3-isoquinolinecarboxylic acid)-8-[L-(2α,3aβ,7aβ)-octahydro-1H-indole-2-carboxylic acid]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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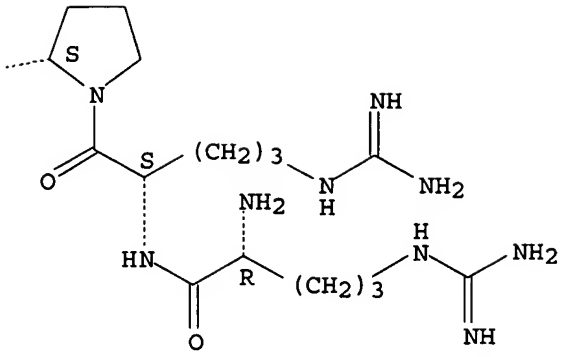
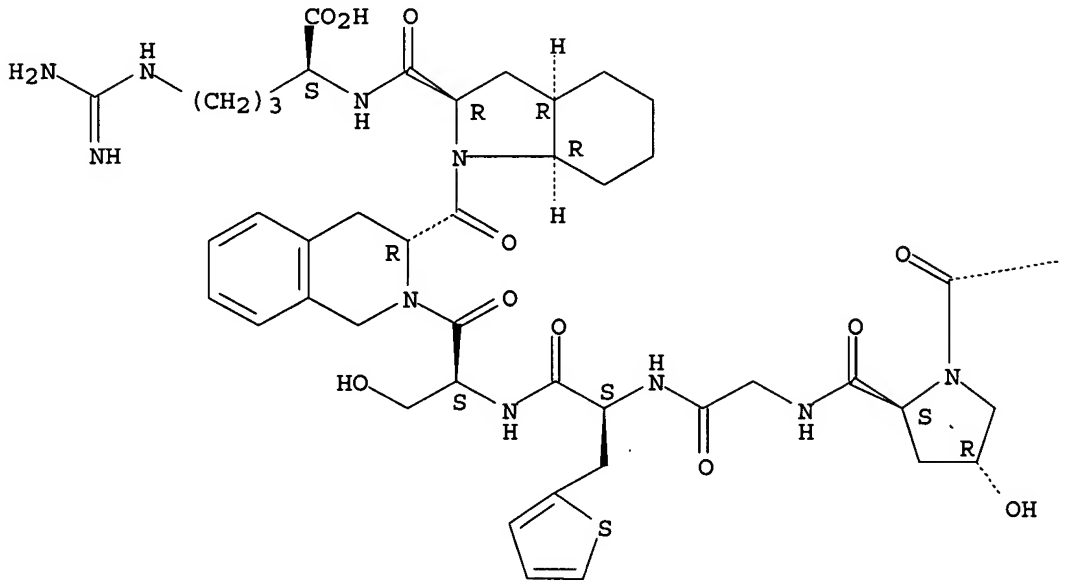


RN 130404-96-5 HCAPLUS
CN L-Arginine, D-arginyl-L-arginyl-L-prolyl-(4R)-4-hydroxy-L-prolylglycyl-3-(2-thienyl)-L-alanyl-L-seryl-(3R)-1,2,3,4-tetrahydro-3-isoquinolinecarbonyl-(2R,3aR,7aR)-octahydro-1H-indole-2-carbonyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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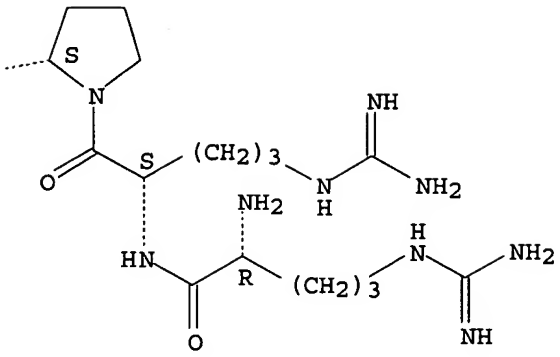


L29 ANSWER 21 OF 21 HCAPLUS COPYRIGHT 2005 ACS on STN
AN 1991:157636 HCAPLUS
DN 114:157636
ED Entered STN: 03 May 1991
TI New, long-acting, potent bradykinin antagonists
AU Lembeck, F.; Greisbacher, T.; Eckhardt, M.; Henke, S.; Breipohl, G.; Knolle, J.
CS Dep. Exp. Clin. Pharmacol., Univ. Graz, Graz, A-8010, Austria
SO British Journal of Pharmacology (**1991**), 102(2), 297-304
CODEN: BJPCBM; ISSN: 0007-1188
DT Journal
LA English
CC 2-10 (Mammalian Hormones)
AB Three new bradykinin (BK) antagonists, D-Arg0-Hyp3-Thi5-D-Tic7-Oic8-BK (where Hyp = hydroxyproline; Thi = β-(2-thienyl)-L-alanine; D-Tic = D-(1,2,3,4-tetrahydroisoquinolin-2-yl-carbonyl) and Oic = L-[(3aS,7aS)-octahydroindol-2-yl-carbonyl]) (I), D-Arg0-Hyp3-D-Tic7-Oic8-BK (II), and Arg(Tos)1-Hyp3-Thi5-D-Tic7-Oic8-BK (where Arg(Tos) = NG-tosyl-L-arginine) (III), were tested against the effects of BK in 9 bioassay prepns. including visceral smooth muscles, vasoconstriction, plasma protein extravasation, release of PGE2, bronchoconstriction, and stimulation of afferent C-fiber nociceptors. In some of these tests the effects of the new compds. were compared with those of the antagonist D-Arg0-Hyp2-Thi5,8-D-Phe7-BK (IV), described by Stewart & Vavrek (1987). For all bioassays the general rank order of potency of the compds. was I > II > III » IV. The new antagonists were long-acting; in some bioassays their effect outlasted the duration of the experiment The inhibitory effects of the new BK antagonists were specific for BK; actions of noradrenaline, angiotensin II, acetylcholine, or histamine were unaffected by the antagonists. They did not stimulate the release of histamine or prostaglandins. An agonistic effect was observed only with very high concns. of I and II in the plasma protein extravasation test. The long duration of action of the new BK antagonists is probably due to a high and long-lasting affinity to the BK receptors. A high resistance of the antagonists to enzymic destruction may be another reason. The new BK

antagonists will be valuable tools for the investigation of the pathophysiol. role of BK. In addition they may offer a potential for therapeutic applications.

ST bradykinin analog antagonist

IT 58-82-2, Bradykinin
RL: BIOL (Biological study)
(antagonists, bradykinin analogs with unusual amino acids as)

IT 103412-36-8 **133162-75-1 133162-76-2** 133162-77-3
RL: BIOL (Biological study)
(as bradykinin antagonist)

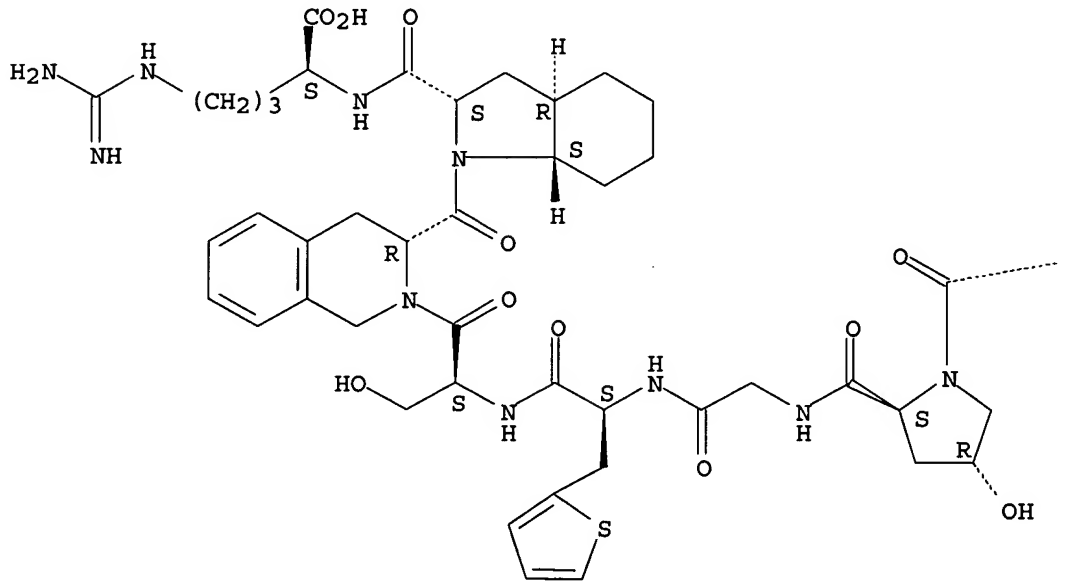
IT **133162-75-1 133162-76-2**
RL: BIOL (Biological study)
(as bradykinin antagonist)

RN 133162-75-1 HCAPLUS

CN L-Arginine, D-arginyl-L-arginyl-L-prolyl-(4R)-4-hydroxy-L-prolylglycyl-3-(2-thienyl)-L-alanyl-L-seryl-(3R)-1,2,3,4-tetrahydro-3-isoquinolinecarbonyl-(2S,3aR,7aS)-octahydro-1H-indole-2-carbonyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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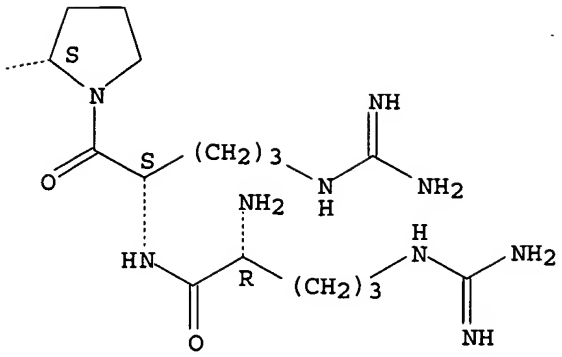
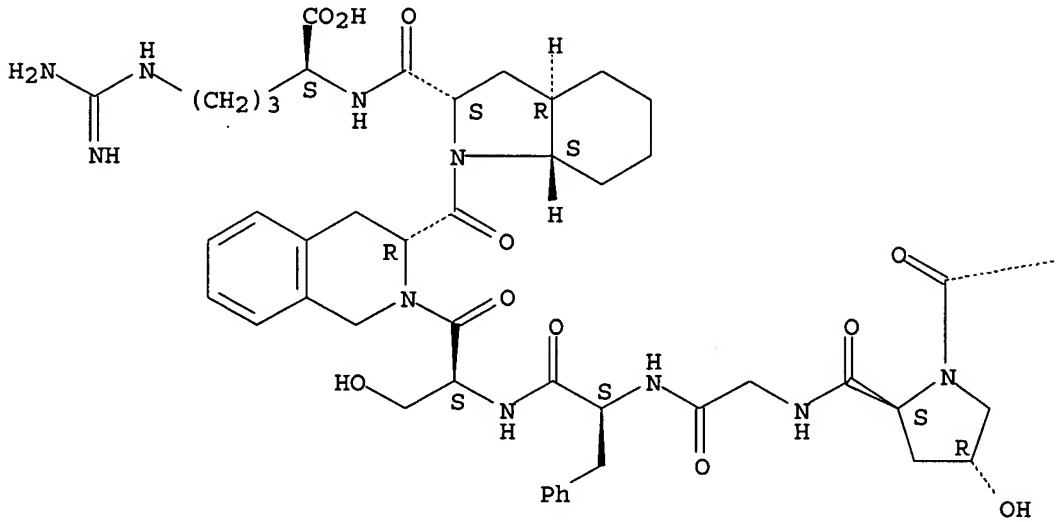


RN 133162-76-2 HCAPLUS
CN Bradykinin, N2-D-arginyl-3-(trans-4-hydroxy-L-proline)-7-(D-1,2,3,4-tetrahydro-3-isoquinolinecarboxylic acid)-8-[L-(2α,3aα,7aβ)-octahydro-1H-indole-2-carboxylic acid]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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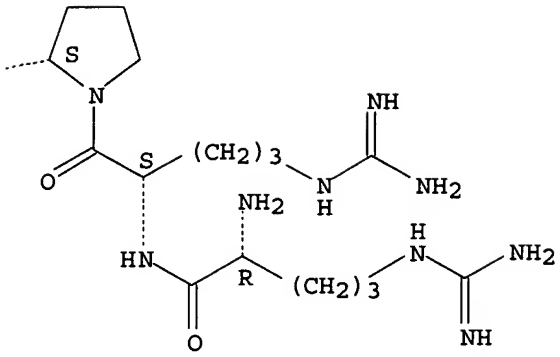

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STRUCTURE FILE UPDATES:   26 SEP 2005  HIGHEST RN 863963-04-6
DICTIONARY FILE UPDATES:  26 SEP 2005  HIGHEST RN 863963-04-6

New CAS Information Use Policies, enter HELP USAGETERMS for details.

TSCA INFORMATION NOW CURRENT THROUGH JULY 14, 2005

  Please note that search-term pricing does apply when
  conducting SmartSELECT searches.

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*                                                                       *
* The CA roles and document type information have been removed from     *
* the IDE default display format and the ED field has been added,       *
* effective March 20, 2005.  A new display format, IDERL, is now        *
* available and contains the CA role and document type information.     *
*                                                                       *
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Structure search iteration limits have been increased.  See HELP SLIMITS
for details.

Experimental and calculated property data are now available. For more
information enter HELP PROP at an arrow prompt in the file or refer
to the file summary sheet on the web at:
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TI Bradykinin-antagonists for the treatment of acute pancreatitis
IN Griesbacher, Thomas, Hitzendorf, Austria
Lembeck, Fred, Graz, Austria
PA Hoechst Aktiengesellschaft, Frankfurt am Main, Germany, Federal Republic of (non-U.S. corporation)
PI US 5670619 19970923
AI US 1994-232338 19940422 (8)
RLI Continuation of Ser. No. US 1992-992096, filed on 17 Dec 1992, now abandoned
PRAI EP 1991-122055 19911221
DT Utility
FS Granted
EXNAM Primary Examiner: Tsang, Cecilia J.; Assistant Examiner: Gupta, Anish
LREP Finnegan, Henderson, Farabow, Garrett & Dunner, L.L.P.
CLMN Number of Claims: 5
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 507
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The invention relates to the use of bradykinin-antagonists of the formula

R.sup.1 -A-B-C-E-F-G-J-K-R.sup.2

wherein R.sup.1 represents hydrogen, C.sub.1 -C.sub.4 -alkanoyl which can be substituted by mercapto, hydroxyphenyl, (4-benzoyl)phenoxy or represents (4-benzoyl)benzoyl-Lys; A represents D-Arg or D-Lys or stands for a direct bond; B represents Arg which can be substituted by NO.sub.2 or toluol-4-sulfonyl or represents Lys which can be substituted by toluol-4-sulfonyl or CO--NH--C.sub.6 H.sub.5, or stands for a direct bond; C represents Hyp-Pro-Gly, Pro-Hyp-Gly, Pro-Pro-Gly or dehydroPro-Hyp-Gly; E represents Thi, Phe, Leu or Cha; F represents Ser or Cys; G represents D-Tic, D-Phe or D-Hyp substituted by C.sub.1 -C.sub.4 -alkoxy; J represents Tic, Aoc or Oic; K represents Arg or Ahx or stands for a direct bond; R.sup.2 is hydroxy or amino; and the physiologically tolerable salts thereof for the treatments of acute pancreatitis, to pharmaceutical agents containing them and to the use thereof for the preparation of appropriate pharmaceutical compositions.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IT **130308-49-5 130334-55-3**
(bradykinin antagonist, for treatment of acyte pancreatitis)

L30 ANSWER 6 OF 6 USPATFULL on STN
AN 97:61666 USPATFULL
TI Peptides having bradykinin antagonist action
IN Henke, Stephan, Hofheim am Taunus, Germany, Federal Republic of
Anagnostopulos, Hiristo, Wiesbaden, Germany, Federal Republic of
Breipohl, Gerhard, Frankfurt am Main, Germany, Federal Republic of
Knolle, Jochen, Kriftel, Germany, Federal Republic of
Stechl, Jens, Frankfurt am Main, Germany, Federal Republic of
Scholkens, Bernward, Kelkeim/Taunus, Germany, Federal Republic of
Fehlhaber, Hans-Wolfram, Idstein, Germany, Federal Republic of
Gerhards, Hermann, Hofheim am Taunus, Germany, Federal Republic of
Hock, Franz, Dieburg, Germany, Federal Republic of
PA Hoechst Aktiengesellschaft, Frankfurt am Main, Germany, Federal Republic of (non-U.S. corporation)
PI US 5648333 19970715
AI US 1995-487442 19950607 (8)
RLI Continuation of Ser. No. US 1994-236018, filed on 2 May 1994 which is a

continuation of Ser. No. US 1993-12849, filed on 3 Feb 1993, now abandoned which is a continuation-in-part of Ser. No. US 1992-982052, filed on 25 Nov 1992, now abandoned Ser. No. Ser. No. US 1992-837090, filed on 18 Feb 1992, now abandoned And Ser. No. US 1992-969523, filed on 30 Oct 1992, now abandoned which is a continuation of Ser. No. US 1992-841766, filed on 2 Mar 1992, now abandoned which is a continuation of Ser. No. US 1991-690297, filed on 24 Apr 1991, now abandoned which is a continuation-in-part of Ser. No. US 1990-565270, filed on 10 Aug 1990, now abandoned which is a continuation-in-part of Ser. No. US 1989-374162, filed on 30 Jun 1989, now abandoned , said Ser. No. US -982052 which is a continuation of Ser. No. US 1991-746149, filed on 14 Aug 1991, now abandoned which is a continuation-in-part of Ser. No. US -374162 , said Ser. No. US -837090 which is a continuation-in-part of Ser. No. US -565270 And Ser. No. US -746149

PRAI DE 1988-3839581 19881124
DE 1989-3916291 19890519
DE 1989-3926225 19890603
DE 1989-3926822 19890814
DE 1990-4013270 19900426

DT Utility
FS Granted
EXNAM Primary Examiner: Tsang, Cecilia J.; Assistant Examiner: Touzeau, P. Lynn
LREP Finnegan, Henderson, Farabow, Garrett & Dunner, L.L.P.
CLMN Number of Claims: 33
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 2227
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Peptides of the formula I

A-B-C-E-F-K-P-G-M-F'-I (I),

wherein the terms A, B, C, E, F, K, P, G, M, F', and I are defined in the specification, have bradykinin antagonist action. Their therapeutic utility includes all pathological states which are mediated, caused or supported by bradykinin and bradykinin-related peptides.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IT **130308-49-5P 130334-55-3P 130404-96-5P**
133162-75-1P 193618-59-6P 193618-60-9P
193618-61-0P 193618-62-1P 193618-63-2P
193618-64-3P 193618-68-7P
(peptides having bradykinin antagonist action)
IT **130308-52-0P 130308-53-1P**
(peptides having bradykinin antagonist action)

=> fil hcaplus
FILE 'HCAPLUS' ENTERED AT 07:31:49 ON 27 SEP 2005
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FILE COVERS 1907 - 27 Sep 2005 VOL 143 ISS 14
FILE LAST UPDATED: 26 Sep 2005 (20050926/ED)

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This file contains CAS Registry Numbers for easy and accurate substance identification.

=> d l29 all hitstr tot

L29 ANSWER 1 OF 21 HCAPLUS COPYRIGHT 2005 ACS on STN
AN 2004:681587 HCAPLUS
DN 141:185137
ED Entered STN: 20 Aug 2004
TI Use of bradykinin B2 receptor antagonists for treating osteoarthritis and other matrix metalloproteinase-associated diseases
IN Michaelis, Martin; Rudolphi, Karl
PA Aventis Pharma Deutschland G.m.b.h., Germany
SO PCT Int. Appl., 16 pp.
CODEN: PIXXD2
DT Patent
LA German
IC ICM A61K038-04
ICS A61P019-00
CC 1-12 (Pharmacology)
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
PI	WO 2004069266	A2	20040819	WO 2004-EP550	20040123	<--
	WO 2004069266	A3	20040930			
	W: AE, AE, AG, AL, AL, AM, AM, AM, AT, AT, AU, AZ, AZ, BA, BB, BG, BG, BR, BR, BW, BY, BY, BZ, BZ, CA, CH, CN, CN, CO, CO, CR, CR, CU, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EC, EC, EE, EE, EG, ES, ES, FI, FI, GB, GD, GE, GE, GH, GM, HR, HR, HU, HU, ID, IL, IN, IS, JP, JP, KE, KE, KG, KG, KP, KP, KP, KR, KR, KZ, KZ, KZ, LC, LK, LR, LS, LS, LT, LU, LV, MA, MD, MD, MG, MK, MN, MW, MX, MX, MZ, MZ, NA, NI					
	RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG					
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	US 2004248809	A1	20041209	US 2004-773772	20040206	<--
PRAI	DE 2003-10304994	A	20030207	<--		
	US 2003-480246P	P	20030620	<--		

CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES	
WO 2004069266	ICM	A61K038-04	
	ICS	A61P019-00	
WO 2004069266	ECLA	A61K038/08	<--
DE 10304994	ECLA	A61K038/08	<--
US 2004248809	NCL	514/015.000	
	ECLA	A61K038/08	<--

OS MARPAT 141:185137
AB Peptides that have a bradykinin-antagonistic effect are suitable for the production of drugs for use in the prophylaxis and therapy of diseases whose progression is associated with an increased activity of matrix metalloproteinases. These diseases include degenerative articular diseases, for example osteoarthritis, spondylosis and chondroporosis after joint trauma or prolonged joint immobilization after meniscus or patella injuries or ruptures of a ligament.
ST bradykinin B2 antagonist degenerative articular disease; osteoarthritis spondylosis chondroporosis bradykinin receptor antagonist; matrix metalloproteinase disease bradykinin B2 antagonist
IT Bradykinin receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(B2; bradykinin B2 receptor antagonists for treating osteoarthritis and other matrix metalloproteinase-associated diseases)
IT Animal cell line
(SW1353; bradykinin B2 receptor antagonists for treating osteoarthritis and other matrix metalloproteinase-associated diseases)
IT Antiarthritics
Human
Osteoarthritis
(bradykinin B2 receptor antagonists for treating osteoarthritis and other matrix metalloproteinase-associated diseases)
IT Cartilage, disease
(degeneration; bradykinin B2 receptor antagonists for treating osteoarthritis and other matrix metalloproteinase-associated diseases)
IT Joint, anatomical
(disease, degeneration; bradykinin B2 receptor antagonists for treating osteoarthritis and other matrix metalloproteinase-associated diseases)
IT Drug delivery systems
(injections, i.p.; bradykinin B2 receptor antagonists for treating osteoarthritis and other matrix metalloproteinase-associated diseases)
IT Drug delivery systems
(injections, i.v.; bradykinin B2 receptor antagonists for treating osteoarthritis and other matrix metalloproteinase-associated diseases)
IT Drug delivery systems
(injections, intraarticular; bradykinin B2 receptor antagonists for treating osteoarthritis and other matrix metalloproteinase-associated diseases)
IT Drug delivery systems
(injections, s.c.; bradykinin B2 receptor antagonists for treating osteoarthritis and other matrix metalloproteinase-associated diseases)
IT Disease, animal
(joint degeneration; bradykinin B2 receptor antagonists for treating osteoarthritis and other matrix metalloproteinase-associated diseases)
IT Immobilization, animal
(joint; bradykinin B2 receptor antagonists for treating osteoarthritis and other matrix metalloproteinase-associated diseases)
IT Joint, anatomical
(meniscus, injury; bradykinin B2 receptor antagonists for treating osteoarthritis and other matrix metalloproteinase-associated diseases)
IT Bone
(patella, injury; bradykinin B2 receptor antagonists for treating osteoarthritis and other matrix metalloproteinase-associated diseases)
IT Inflammation
Spinal column, disease
(spondylitis; bradykinin B2 receptor antagonists for treating osteoarthritis and other matrix metalloproteinase-associated diseases)
IT Ligament
(torn; bradykinin B2 receptor antagonists for treating osteoarthritis

and other matrix metalloproteinase-associated diseases)

IT Drug delivery systems
(transdermal; bradykinin B2 receptor antagonists for treating osteoarthritis and other matrix metalloproteinase-associated diseases)

IT Joint, anatomical
(trauma; bradykinin B2 receptor antagonists for treating osteoarthritis and other matrix metalloproteinase-associated diseases)

IT 79955-99-0, Matrix metalloproteinase 3
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(bradykinin B2 receptor antagonists for treating osteoarthritis and other matrix metalloproteinase-associated diseases)

IT **130308-49-5 199870-83-2 740808-61-1**
740808-62-2 740808-63-3 740808-64-4
RL: PAC (Pharmacological activity); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(bradykinin B2 receptor antagonists for treating osteoarthritis and other matrix metalloproteinase-associated diseases)

IT **130308-49-5 199870-83-2 740808-61-1**
740808-62-2 740808-63-3 740808-64-4
RL: PAC (Pharmacological activity); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(bradykinin B2 receptor antagonists for treating osteoarthritis and other matrix metalloproteinase-associated diseases)

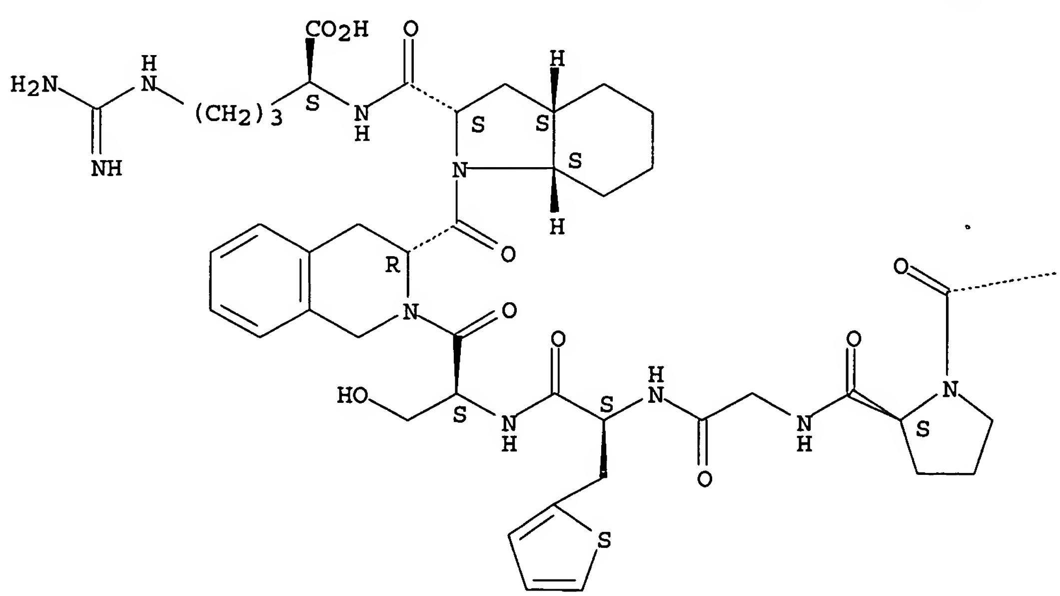
IT **130308-49-5 199870-83-2 740808-61-1**
740808-62-2 740808-63-3 740808-64-4
RL: PAC (Pharmacological activity); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(bradykinin B2 receptor antagonists for treating osteoarthritis and other matrix metalloproteinase-associated diseases)

RN 130308-49-5 HCAPLUS

CN L-Arginine, D-arginyl-L-arginyl-L-prolyl-L-prolylglycyl-3-(2-thienyl)-L-alanyl-L-seryl-(3R)-1,2,3,4-tetrahydro-3-isoquinolinecarbonyl-(2S,3aS,7aS)-octahydro-1H-indole-2-carbonyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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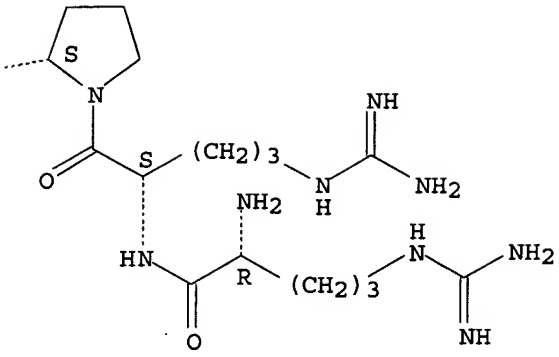
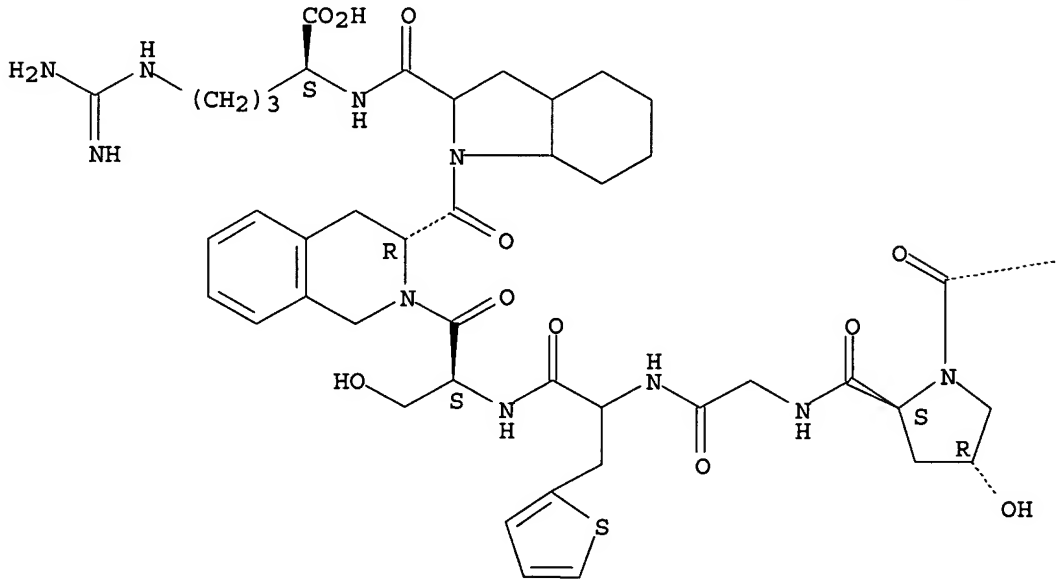


RN 199870-83-2 HCAPLUS
CN L-Arginine, D-arginyl-L-arginyl-L-prolyl-(4R)-4-hydroxy-L-prolylglycyl-3-(2-thienyl)alanyl-L-seryl-(3R)-1,2,3,4-tetrahydro-3-isoquinolinecarbonyloctahydro-1H-indole-2-carbonyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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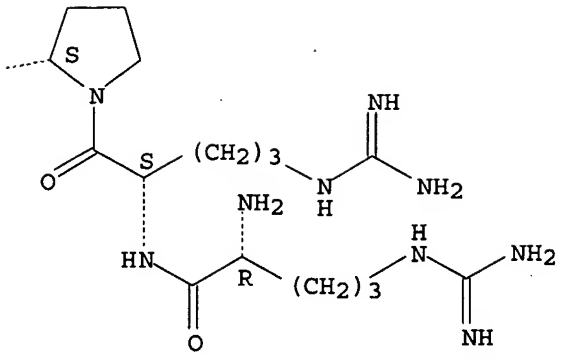

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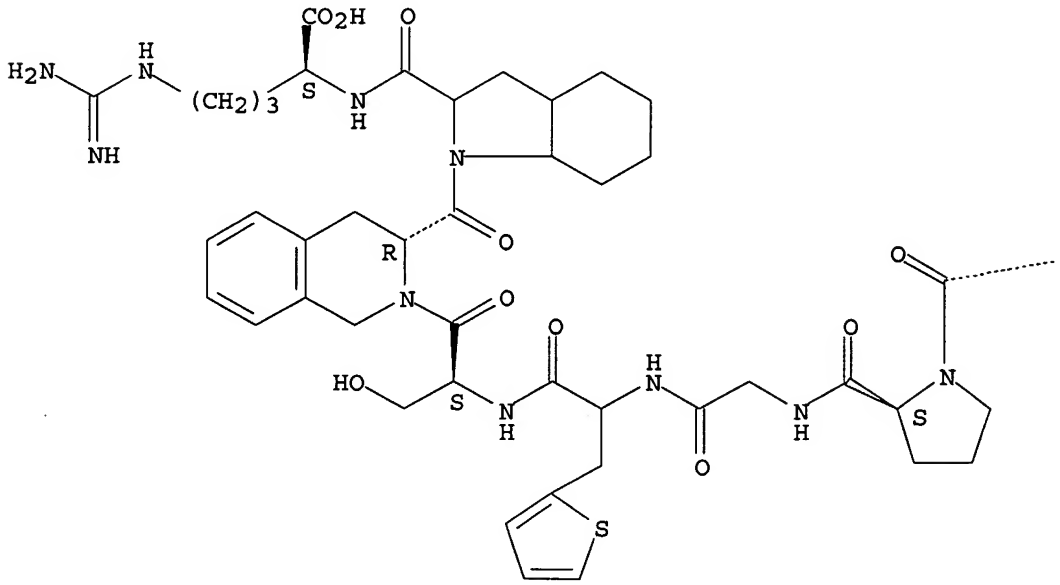
CN L-Arginine, D-arginyl-L-arginyl-L-prolyl-L-prolylglycyl-3-(2-thienyl)alanyl-L-seryl-(3R)-1,2,3,4-tetrahydro-3-isoquinolinecarbonyloctahydro-1H-indole-2-carbonyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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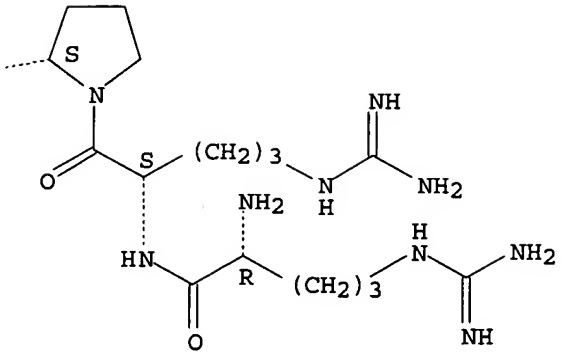

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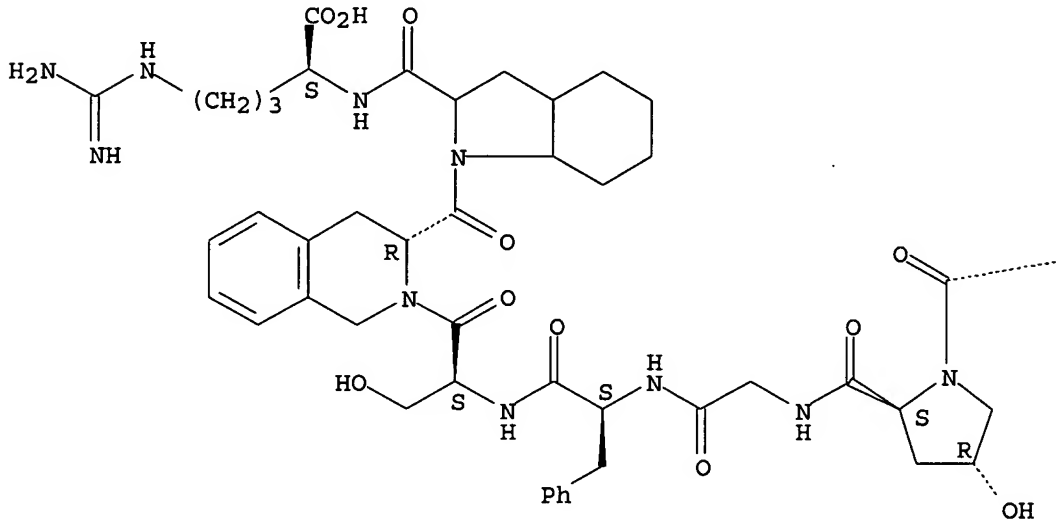
CN L-Arginine, D-arginyl-L-arginyl-L-prolyl-(4R)-4-hydroxy-L-prolylglycyl-L-phenylalanyl-L-seryl-(3R)-1,2,3,4-tetrahydro-3-isoquinolinecarbonyloctahydro-1H-indole-2-carbonyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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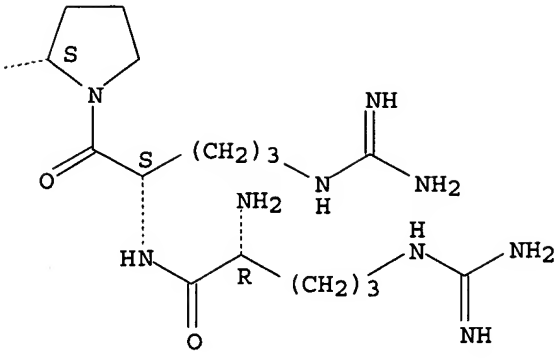

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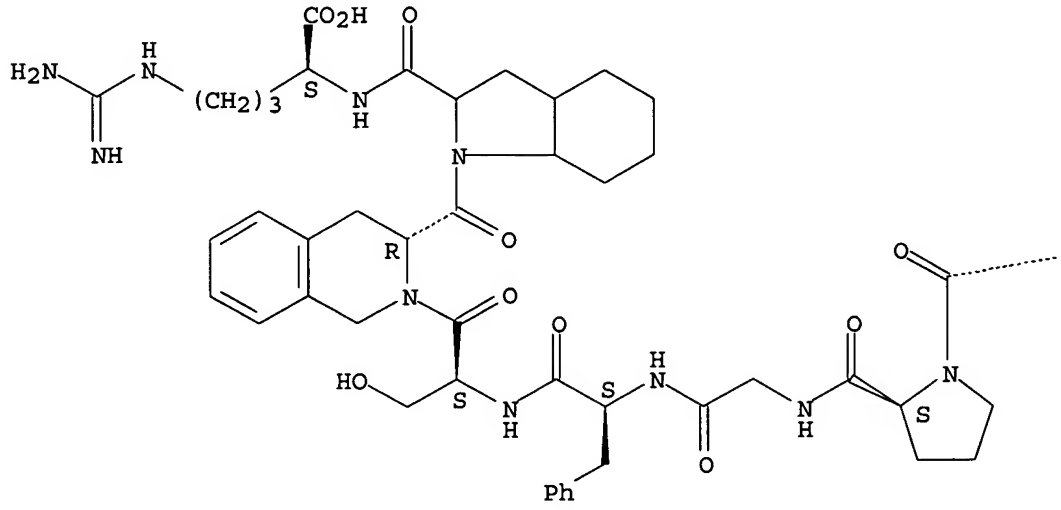
Absolute stereochemistry.

PAGE 1-A



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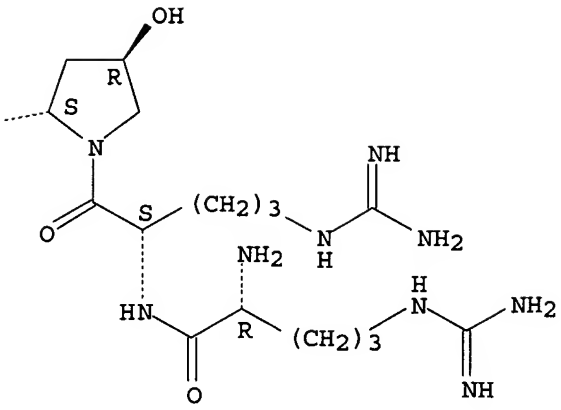
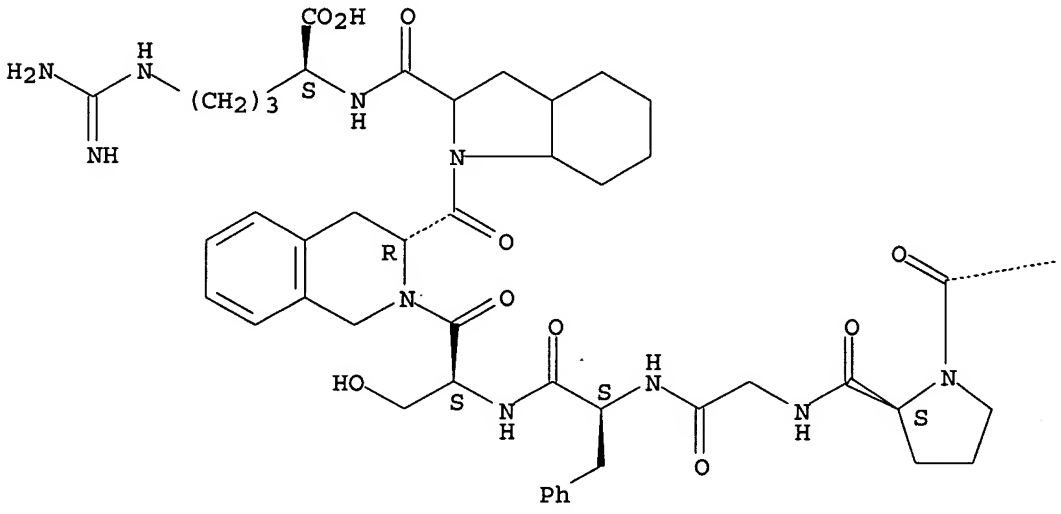


RN 740808-64-4 HCAPLUS
CN L-Arginine, D-arginyl-L-arginyl-L-prolyl-L-prolylglycyl-L-phenylalanyl-L-seryl-(3R)-1,2,3,4-tetrahydro-3-isoquinolinecarbonyloctahydro-1H-indole-2-carbonyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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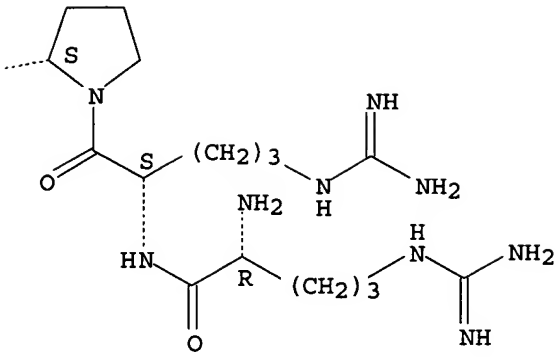
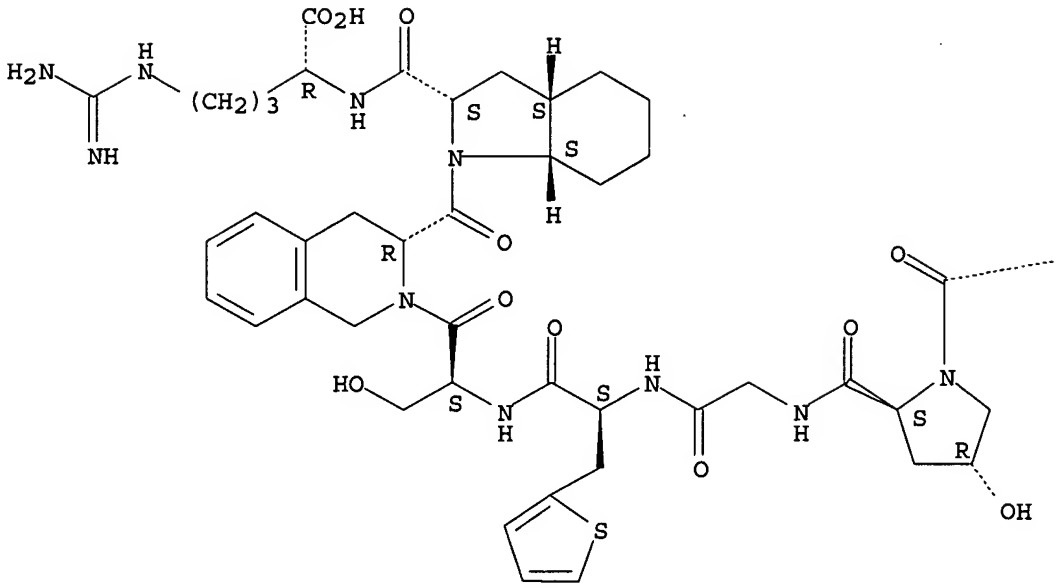


L29 ANSWER 2 OF 21 HCAPLUS COPYRIGHT 2005 ACS on STN
AN 2004:28296 HCAPLUS
DN 141:151157
ED Entered STN: 14 Jan 2004
TI New constrained amino acids for the study of the role of the basic residues in bradykinin antagonists
AU Alcaro, Maria C.; Terzani, Tullio; Nuti, Francesca; Chelli, Mario; Machetti, Fabrizio; Quartara, Laura; Patacchini, Riccardo; Meini, Stefania; Giuliani, Sandro; Brandi, Alberto; Rovero, Paolo; Papini, Anna M.
CS Dipartimento di Chimica Organica "Ugo Schiff", Universita di Firenze and CNR-ICCOM, Sesto Fiorentino (FI), I-50019, Italy
SO Peptides 2002, Proceedings of the European Peptide Symposium, 27th, Sorrento, Italy, Aug. 31-Sept. 6, 2002 (**2002**), 18-19.
Editor(s): Benedetti, Ettore; Pedone, Carlo. Publisher: Edizioni Ziino, Castellammare di Stabia, Italy.
CODEN: 69EYXG; ISBN: 88-900948-1-8
DT Conference
LA English
CC 2-2 (Mammalian Hormones)
Section cross-reference(s): 34
AB Several antagonists for the bradykinin B2 receptor have been developed. Among these the second-generation peptide HOE 140 (H-D-Arg0-Arg1-Pro2-Hyp3-Gly4-Thi5-Ser6-D-Tic7-Oic8-Arg9-OH) represents the model for the preparation of highly potent compds. To investigate the role of the basic residues H-D-Arg0-Arg1 and Arg9-OH in the activity of HOE 140, a series of HOE 140 peptide analogs modified at the N- and C-terminal positions were prepared and tested for bradykinin B2 receptor antagonist activity. All the peptides showed a less potent antagonist activity at the B2 receptor than HOE 140. It seems that for a good binding to the B2 receptor the amino acids responsible for the basic interaction should possess an aliphatic chain whose length is longer than Orn and shorter than Lys, and whose direction is that imposed by an L-stereochem. The preparation of Fmoc-Api(Boc)-OH is described.
ST HOE 140 peptide analog bradykinin B2 receptor antagonist

IT Bradykinin receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(B2; new constrained amino acids for study of role of basic residues in peptide analogs of HOE 140 as bradykinin antagonists)
IT Structure-activity relationship
(bradykinin-inhibiting; new constrained amino acids for study of role of basic residues in peptide analogs of HOE 140 as bradykinin antagonists)
IT 58-82-2, Bradykinin
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(new constrained amino acids for study of role of basic residues in peptide analogs of HOE 140 as bradykinin antagonists)
IT 130389-50-3, MEN 11661 138614-30-9, HOE 140 **193618-62-1**, MEN 11646 506441-29-8, MEN 11670 729558-81-0, MEN 11632 729558-82-1, MEN 11659 729558-83-2, MEN 11658 729558-84-3, MEN 11747 729558-85-4, MEN 11748 729558-86-5, MEN 11692 729558-87-6, MEN 11746 729558-88-7, MEN 11766 729558-89-8, TTBK
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(new constrained amino acids for study of role of basic residues in peptide analogs of HOE 140 as bradykinin antagonists)
IT 357154-19-9
RL: RCT (Reactant); RACT (Reactant or reagent)
(new constrained amino acids for study of role of basic residues in peptide analogs of HOE 140 as bradykinin antagonists)
IT 728946-36-9P 728946-37-0P 728946-38-1P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(new constrained amino acids for study of role of basic residues in peptide analogs of HOE 140 as bradykinin antagonists)
RE.CNT 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
(1) Guba, W; J Am Chem Soc 1994, V116, P7532 HCAPLUS
(2) Kennedy, K; J Peptide Res 2002, V59, P139 HCAPLUS
(3) Machetti, F; Tetrahedron 2001, V57, P4995 HCAPLUS
(4) York, E; Peptides:The Wave of the Future (Proceedings of the 2nd International Peptide Symposium and the 17th American Peptide Symposium) 2001, P721 HCAPLUS
IT **193618-62-1**, MEN 11646
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(new constrained amino acids for study of role of basic residues in peptide analogs of HOE 140 as bradykinin antagonists)
RN 193618-62-1 HCAPLUS
CN D-Arginine, D-arginyl-L-arginyl-L-prolyl-(4R)-4-hydroxy-L-prolylglycyl-3-(2-thienyl)-L-alanyl-L-seryl-(3R)-1,2,3,4-tetrahydro-3-isoquinolinecarbonyl-(2S,3aS,7aS)-octahydro-1H-indole-2-carbonyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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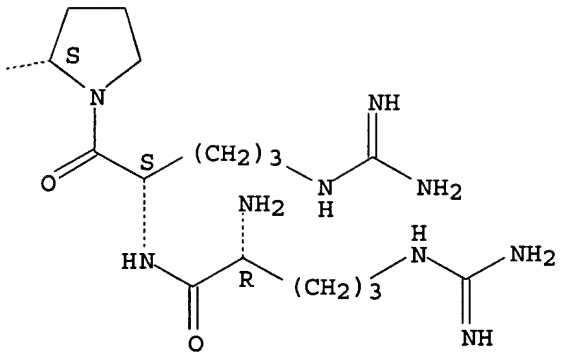

L29 ANSWER 3 OF 21 HCAPLUS COPYRIGHT 2005 ACS on STN
AN 2003:737369 HCAPLUS
DN 139:255368
ED Entered STN: 19 Sep 2003
TI Prokinetic agents for treating gastric hypomotility and related disorders
IN Watson, John W.; Andrews, Paul L. R.; Woods, Anthony J.
PA USA
SO U.S. Pat. Appl. Publ., 57 pp.

CODEN: USXXCO
DT Patent
LA English
IC ICM A61K031-542
ICS A61K031-538; A61K031-497; A61K031-541; A61K031-53; A61K031-52; A61K031-517
INCL 514224200; 514242000; 514263200; 514254060; 514251000; 514255050; 514233500; 514300000; 514256000; 514266230
CC 1-9 (Pharmacology)
Section cross-reference(s): 28, 63
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2003176421	A1	20030918	US 1999-476253	19991230 <--

PRAI US 1999-476253 19991230 <--

CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
US 2003176421	ICM	A61K031-542
	ICS	A61K031-538; A61K031-497; A61K031-541; A61K031-53; A61K031-52; A61K031-517
	INCL	514224200; 514242000; 514263200; 514254060; 514251000; 514255050; 514233500; 514300000; 514256000; 514266230
US 2003176421	NCL	514/224.200 <--

OS MARPAT 139:255368
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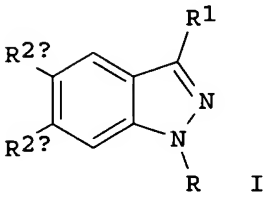

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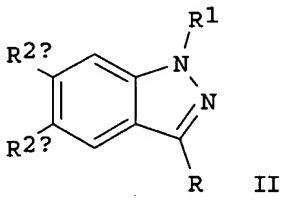


II

AB Stasis is treated or prevented in all or any part or parts of the stomach of a patient, especially a human patient, in need of such treatment, where said stasis results from hypomotility in the stomach, particularly gastric hypomotility with delayed emptying of the liquid and/or solid contents of the stomach. Gastric or gastrointestinal disorders are also treated which are characterized by one or more symptoms selected from pain, nausea, vomiting, heartburn, postprandial discomfort, indigestion and gastroesophageal reflux. Such treatment or prevention is achieved by administering to the patient a therapeutically effective amount of an inhibitor of phosphodiesterase-4 (PDE4), including isoenzyme subtypes thereof, sufficient to treat or prevent such hypomotility or gastric or gastrointestinal disorder in said patient. The PDE4 inhibitor comprises I or II [preferrably R = cyclopentyl or cyclohexyl; R1 = (C1-C2) alkyl; one of R2a and R2b = H and the other = Q; dashed line = single bond; m = 0, R113 and R114 are cis to each other; R113 = CN, R115 = H, R114 = carboxy, -CH2OH, -CH2C(=O)NH2]. Pharmaceutical compns. are also described which are useful for carrying out the above-mentioned methods of treatment and prevention, and which are also useful in the treatment of a gastric or gastrointestinal disorder in a patient which comprises with respect to said patient, (i) a sign or concomitant of diabetic neuropathy, anorexia

nervosa, achlorhydria, gastrointestinal surgery, post-surgical recovery in the period of emergence from general anesthesia; or the administration of morphine and morphine-like opioids; (ii) a secondary aspect of a primary disease or disorder in said patient which is organic, wherein said disease or disorder involves particularly a gastroenteric or gastroesophageal organ or tissue, or an organ or tissue of the central nervous system of said patient; or (iii) an adverse side effect of a different therapeutic agent administered to said patient in the course of treating another unrelated disease or disorder in said patient.

ST prokinetic agent treatment gastric hypomotility; phosphodiesterase 4 inhibitor prokinetic agent gastrointestinal disorder

IT Antihistamines
(H1, pharmaceutical containing phosphodiesterase-4 inhibitor and; prokinetic phosphodiesterase-4 inhibitor agents for treating gastric hypomotility and related disorders)

IT Stomach, disease
(anacidity, gastrointestinal disorder in relation to; prokinetic phosphodiesterase-4 inhibitor agents for treating gastric hypomotility and related disorders)

IT Enkephalins
Opioids
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(analgesics, as auxiliary therapeutic agents; prokinetic phosphodiesterase-4 inhibitor agents for treating gastric hypomotility and related disorders)

IT Appetite
(anorexia nervosa, gastrointestinal disorder in relation to; prokinetic phosphodiesterase-4 inhibitor agents for treating gastric hypomotility and related disorders)

IT Corticosteroids, biological studies
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(anti-inflammatory, as auxiliary therapeutic agents; prokinetic phosphodiesterase-4 inhibitor agents for treating gastric hypomotility and related disorders)

IT Interleukin 1
Interleukin 10
Interleukin 11
Interleukin 12
Interleukin 2
Interleukin 3
Interleukin 4
Interleukin 5
Interleukin 6
Interleukin 7
Interleukin 8
Interleukin 9
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(as auxiliary therapeutic agent; prokinetic phosphodiesterase-4 inhibitor agents for treating gastric hypomotility and related disorders)

IT Cholinergic antagonists
Leukotriene antagonists
Thromboxane receptor antagonists
(as auxiliary therapeutic agents; prokinetic phosphodiesterase-4 inhibitor agents for treating gastric hypomotility and related disorders)

IT Cytokines

Interleukins
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(as auxiliary therapeutic agents; prokinetic phosphodiesterase-4 inhibitor agents for treating gastric hypomotility and related disorders)

IT Nausea
Pain
Vomiting
(as symptom of gastrointestinal disorders; prokinetic phosphodiesterase-4 inhibitor agents for treating gastric hypomotility and related disorders)

IT Diuretics
(causing hypokalemia, pharmaceutical containing phosphodiesterase-4 inhibitor and; prokinetic phosphodiesterase-4 inhibitor agents for treating gastric hypomotility and related disorders)

IT Inflammation
(chronic, autocoids for treatment of pain and, as auxiliary therapeutic agents; prokinetic phosphodiesterase-4 inhibitor agents for treating gastric hypomotility and related disorders)

IT Anti-inflammatory agents
(corticosteroids, as auxiliary therapeutic agents; prokinetic phosphodiesterase-4 inhibitor agents for treating gastric hypomotility and related disorders)

IT Nerve, disease
(diabetic neuropathy, gastrointestinal disorder in relation to; prokinetic phosphodiesterase-4 inhibitor agents for treating gastric hypomotility and related disorders)

IT Postprandial period
(discomfort, as symptom of gastrointestinal disorders; prokinetic phosphodiesterase-4 inhibitor agents for treating gastric hypomotility and related disorders)

IT Gastrointestinal motility
(disorder, dysmotility; prokinetic phosphodiesterase-4 inhibitor agents for treating gastric hypomotility and related disorders)

IT Opioids
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(endogenous, proteinaceous analgesics, as auxiliary therapeutic agents; prokinetic phosphodiesterase-4 inhibitor agents for treating gastric hypomotility and related disorders)

IT Nervous system agents
(ganglionic blocking agents, pharmaceutical containing phosphodiesterase-4 inhibitor and; prokinetic phosphodiesterase-4 inhibitor agents for treating gastric hypomotility and related disorders)

IT Digestive tract, disease
(gastroesophageal reflux, as symptom of gastrointestinal disorders; prokinetic phosphodiesterase-4 inhibitor agents for treating gastric hypomotility and related disorders)

IT Therapy
(gastrointestinal disorder from; prokinetic phosphodiesterase-4 inhibitor agents for treating gastric hypomotility and related disorders)

IT Surgery
(gastrointestinal, gastrointestinal disorder in relation to; prokinetic phosphodiesterase-4 inhibitor agents for treating gastric hypomotility and related disorders)

IT Anesthesia
(general, post-surgical recovery in period of emergence from, gastrointestinal disorder in relation to; prokinetic

phosphodiesterase-4 inhibitor agents for treating gastric hypomotility and related disorders)
IT Digestive tract, disease
(indigestion, as symptom of gastrointestinal disorders; prokinetic phosphodiesterase-4 inhibitor agents for treating gastric hypomotility and related disorders)
IT Drug delivery systems
(inhalants, anti-inflammatory corticosteroids, as auxiliary therapeutic agents; prokinetic phosphodiesterase-4 inhibitor agents for treating gastric hypomotility and related disorders)
IT Drug delivery systems
(injections, anti-inflammatory corticosteroids, as auxiliary therapeutic agents; prokinetic phosphodiesterase-4 inhibitor agents for treating gastric hypomotility and related disorders)
IT Opioids
RL: ADV (Adverse effect, including toxicity); BSU (Biological study, unclassified); BIOL (Biological study)
(morphine-like, gastrointestinal disorder from; prokinetic phosphodiesterase-4 inhibitor agents for treating gastric hypomotility and related disorders)
IT Digestive tract, disease
Stomach, disease
(motility disorders; prokinetic phosphodiesterase-4 inhibitor agents for treating gastric hypomotility and related disorders)
IT Drug delivery systems
(nasal, anti-inflammatory corticosteroids, as auxiliary therapeutic agents; prokinetic phosphodiesterase-4 inhibitor agents for treating gastric hypomotility and related disorders)
IT Analgesics
Anti-inflammatory agents
Antipyretics
(nonsteroidal, as auxiliary therapeutic agents; prokinetic phosphodiesterase-4 inhibitor agents for treating gastric hypomotility and related disorders)
IT Gastric emptying
(of liqs. and/or solids, delayed; prokinetic phosphodiesterase-4 inhibitor agents for treating gastric hypomotility and related disorders)
IT Drug delivery systems
(ophthalmic, anti-inflammatory corticosteroids, as auxiliary therapeutic agents; prokinetic phosphodiesterase-4 inhibitor agents for treating gastric hypomotility and related disorders)
IT Proteins
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(opioid analgesics, as auxiliary therapeutic agents; prokinetic phosphodiesterase-4 inhibitor agents for treating gastric hypomotility and related disorders)
IT Analgesics
(opioid, as auxiliary therapeutic agents; prokinetic phosphodiesterase-4 inhibitor agents for treating gastric hypomotility and related disorders)
IT Drug delivery systems
(oral, anti-inflammatory corticosteroids, as auxiliary therapeutic agents; prokinetic phosphodiesterase-4 inhibitor agents for treating gastric hypomotility and related disorders)
IT Antacids
Antidiarrheals
Antiparkinsonian agents
Laxatives

Muscle relaxants
(pharmaceutical containing phosphodiesterase-4 inhibitor and; prokinetic phosphodiesterase-4 inhibitor agents for treating gastric hypomotility and related disorders)

IT Corticosteroids, biological studies
Heavy metals
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pharmaceutical containing phosphodiesterase-4 inhibitor and; prokinetic phosphodiesterase-4 inhibitor agents for treating gastric hypomotility and related disorders)

IT Drug delivery systems
Gastrointestinal motility
Human
Mammalia
Prokinetic agents
(prokinetic phosphodiesterase-4 inhibitor agents for treating gastric hypomotility and related disorders)

IT Hormone antagonists
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(prostaglandin antagonists, analgesics, pharmaceutical containing phosphodiesterase-4 inhibitor and; prokinetic phosphodiesterase-4 inhibitor agents for treating gastric hypomotility and related disorders)

IT Digestive tract, disease
(pyrosis, as symptom of gastrointestinal disorders; prokinetic phosphodiesterase-4 inhibitor agents for treating gastric hypomotility and related disorders)

IT Drug delivery systems
(topical, anti-inflammatory corticosteroids, as auxiliary therapeutic agents; prokinetic phosphodiesterase-4 inhibitor agents for treating gastric hypomotility and related disorders)

IT Anti-inflammatory agents
(topical, corticosteroids, as auxiliary therapeutic agents; prokinetic phosphodiesterase-4 inhibitor agents for treating gastric hypomotility and related disorders)

IT Antidepressants
(tricyclic, with anticholinergic effect, pharmaceutical containing phosphodiesterase-4 inhibitor and; prokinetic phosphodiesterase-4 inhibitor agents for treating gastric hypomotility and related disorders)

IT Antihistamines
(with anticholinergic effect, pharmaceutical containing phosphodiesterase-4 inhibitor and; prokinetic phosphodiesterase-4 inhibitor agents for treating gastric hypomotility and related disorders)

IT Opioid receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(κ-opioid, proteinaceous opioid analgesic agonists and antagonists of, as auxiliary therapeutic agents; prokinetic phosphodiesterase-4 inhibitor agents for treating gastric hypomotility and related disorders)

IT Opioid antagonists
(κ-opioid, proteinaceous opioid analgesics, as auxiliary therapeutic agents; prokinetic phosphodiesterase-4 inhibitor agents for treating gastric hypomotility and related disorders)

IT Opioid receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(δ-opioid, proteinaceous opioid analgesic agonists and antagonists of, as auxiliary therapeutic agents; prokinetic

phosphodiesterase-4 inhibitor agents for treating gastric hypomotility and related disorders)

IT Opioid antagonists
(δ-opioid, proteinaceous opioid analgesics, as auxiliary therapeutic agents; prokinetic phosphodiesterase-4 inhibitor agents for treating gastric hypomotility and related disorders)

IT Opioid receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(μ-opioid, proteinaceous opioid analgesic agonists and antagonists of, as auxiliary therapeutic agents; prokinetic phosphodiesterase-4 inhibitor agents for treating gastric hypomotility and related disorders)

IT Opioid antagonists
(μ-opioid, proteinaceous opioid analgesics, as auxiliary therapeutic agents; prokinetic phosphodiesterase-4 inhibitor agents for treating gastric hypomotility and related disorders)

IT 199171-80-7 199171-81-8 199171-82-9 199171-83-0 199171-84-1
199171-85-2 199171-86-3 199171-87-4 199171-88-5 199171-89-6
199171-90-9 199171-91-0 199171-92-1 224048-00-4 224048-01-5
224048-02-6 224048-03-7 224048-05-9 224048-06-0 224048-07-1
224048-08-2 224048-09-3 224048-10-6 224048-11-7 224048-13-9
224048-14-0 224048-15-1 224048-21-9 224048-23-1 284465-42-5
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(PDE4 inhibitor; prokinetic phosphodiesterase-4 inhibitor agents for treating gastric hypomotility and related disorders)

IT 60118-07-2D, Endorphin, compds. 74913-18-1D, Dynorphin, compds.
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(analgesics, as auxiliary therapeutic agents; prokinetic phosphodiesterase-4 inhibitor agents for treating gastric hypomotility and related disorders)

IT 471-34-1, Calcium carbonate, biological studies 21645-51-2, Aluminum hydroxide, biological studies
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(antacids, pharmaceutical containing phosphodiesterase-4 inhibitor and; prokinetic phosphodiesterase-4 inhibitor agents for treating gastric hypomotility and related disorders)

IT 15958-92-6, 1-8-Bradykinin 58569-55-4, (Met5)enkephalin 58822-25-6, 1-5-β-Neoendorphin (human) 63631-40-3, (D-Ala2,D-Leu5)enkephalin 64695-06-3 71800-36-7, 1-9-Kallidin 73742-30-0 74135-04-9, Morphiceptin 75644-90-5, (D-Ser2,Leu5)enkephalin-Thr6 78123-71-4 83397-56-2 88373-73-3, (D-Pen2,D-Pen5)enkephalin 97825-00-8 110881-59-9 122752-15-2, Deltorphin C 122752-16-3, Deltorphin B 288570-66-1 **603969-58-0**
RL: PAC (Pharmacological activity); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(as auxiliary therapeutic agent; prokinetic phosphodiesterase-4 inhibitor agents for treating gastric hypomotility and related disorders)

IT 50-02-2, Dexamethasone 50-03-3, Cortisol acetate 50-04-4, Cortisone acetate 50-13-5, Meperidine hydrochloride 50-23-7, Cortisol 50-24-8, Prednisolone 50-33-9, Phenylbutazone, biological studies 50-78-2, Aspirin 52-21-1, Prednisolone acetate 52-28-8, Codeine phosphate 53-03-2, Prednisone 53-36-1, Methylprednisolone acetate 53-86-1, Indomethacin 54-21-7, Sodium salicylate 58-82-2, Bradykinin 61-68-7, Mefenamic acid 64-31-3, Morphine sulfate 67-73-2, Fluocinolone acetonide 67-78-7, Triamcinolone diacetate 71-68-1, Hydromorphone hydrochloride 76-25-5, Triamcinolone acetonide 76-42-6, Oxycodone

76-57-3, Codeine 83-43-2, Methylprednisolone 103-90-2, Acetaminophen 119-36-8, Methyl salicylate 124-90-3, Oxycodone hydrochloride 124-94-7, Triamcinolone 125-02-0, Prednisolone sodium phosphate 125-04-2, Cortisol sodium succinate 125-72-4, Levorphanol tartrate 126-12-5, Anileridine hydrochloride 144-14-9, Anileridine 151-73-5, Betamethasone sodium phosphate 342-10-9, Kallidin 356-12-7, Fluocinonide 357-07-3, Oxymorphone hydrochloride 378-44-9, Betamethasone 382-67-2, Desoximetasone 426-13-1, Fluorometholone 508-99-6, Cortisol cypionate 509-74-0, Methadyl acetate 514-36-3, Fludrocortisone acetate 530-78-9, Flufenamic acid 552-94-3, Salsalate 599-79-1, Sulfasalazine 638-94-8, Desonide 644-62-2, Meclofenamic acid 990-73-8, Fentanyl citrate 1095-90-5, Methadone hydrochloride 1177-87-3, Dexamethasone acetate 1420-53-7, Codeine sulfate 1477-40-3, Levomethadyl acetate 1524-88-5, Flurandrenolide 1597-82-6, Paramethasone acetate 2152-44-5, Betamethasone valerate 2375-03-3, Methylprednisolone sodium succinate 2392-39-4, Dexamethasone sodium phosphate 2668-66-8, Medrysone 3093-35-4, Halcinonide 3385-03-3, Flunisolide 5104-49-4, Flurbiprofen 5534-09-8, Beclomethasone dipropionate 5593-20-4, Betamethasone dipropionate 5611-51-8, Triamcinolone hexacetonide 6000-74-4, Cortisol sodium phosphate 6677-99-2 6678-00-8 7681-14-3, Prednisolone tebutate 8064-08-2 13539-59-8, Apazone 13710-19-5, Tolfenamic acid 15307-86-5, Diclofenac 15687-27-1, Ibuprofen 15722-48-2, Olsalazine 21256-18-8, Oxaprozin 22071-15-4, Ketoprofen 22204-53-1, Naproxen 22254-24-6, Ipratropium bromide 22298-29-9, Betamethasone benzoate 22494-42-4, Diflunisal 25122-46-7, Clobetasol propionate 25333-72-6, Oxycodone terephthalate 26171-23-3, Tolmetin 29679-58-1, Fenoprofen 33564-31-7, Diflorasone diacetate 34097-16-0, Clocortolone pivalate 36322-90-4, Piroxicam 38194-50-2, Sulindac 41340-25-4, Etodolac 42924-53-8, Nabumetone 43033-72-3, Levomethadyl acetate hydrochloride 51022-69-6, Amcinonide 51803-78-2, Nimesulide 59804-37-4, Tenoxicam 60561-17-3, Sufentanil citrate 61380-27-6, Carfentanil citrate 61380-41-4, Lofentanil oxalate 64425-90-7, Choline magnesium trisalicylate, biological studies 66734-13-2, Alclometasone dipropionate 68616-83-1, Pentamorphone 69049-06-5, Alfentanil hydrochloride 69671-17-6, α-Neoendorphin 71125-38-7, Meloxicam 74103-06-3, Ketorolac 77752-00-2, β-Neoendorphin 80809-81-0, Docebenone 83869-56-1, Granulocyte-macrophage colony-stimulating factor 83919-23-7, Mometasone furoate 85006-82-2, Dynorphin B 88107-10-2, Tomelukast 88161-22-2, Dynorphin A 96565-55-8, Ablukast sodium 96566-25-5, Ablukast 98116-53-1, Sulukast 103177-37-3, Pranlukast 107753-78-6, Zafirlukast 111406-87-2, Zileuton 111974-60-8, Ritolukast 112665-43-7, Seratrodast 112964-97-3, Ocfentanil hydrochloride 117268-95-8, Brifentanil hydrochloride 120210-48-2, Tenidap 120443-16-5, Verlukast 128312-51-6, Cinalukast 132956-22-0, Enazadrem phosphate 143011-72-7, Granulocyte-colony stimulating factor 147432-77-7, Ontazolast 151581-24-7, Iralukast 151767-02-1, Montelukast sodium 385390-37-4, Pobilukast edamine
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(as auxiliary therapeutic agent; prokinetic phosphodiesterase-4 inhibitor agents for treating gastric hypomotility and related disorders)

IT 64-19-7D, Acetic acid, hetoaryl derivs. 69-72-7D, Salicylic acid, derivs. 79-09-4D, Propionic acid, aryl compds. 87-51-4D, Indole acetic acid, derivs. 118-92-3D, Anthranilic acid, derivs. 123-30-8D, derivs. 62683-29-8, Colony-stimulating factor
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(as auxiliary therapeutic agents; prokinetic phosphodiesterase-4

inhibitor agents for treating gastric hypomotility and related disorders)

IT 57-27-2, Morphine, biological studies
RL: ADV (Adverse effect, including toxicity); BSU (Biological study, unclassified); BIOL (Biological study)
(gastrointestinal disorder from; prokinetic phosphodiesterase-4 inhibitor agents for treating gastric hypomotility and related disorders)

IT 7440-09-7, Potassium, biological studies
RL: ADV (Adverse effect, including toxicity); BSU (Biological study, unclassified); BIOL (Biological study)
(hypokalemia, pharmaceutical containing phosphodiesterase-4 inhibitor and diuretics causing; prokinetic phosphodiesterase-4 inhibitor agents for treating gastric hypomotility and related disorders)

IT 80619-02-9, 5-Lipoxygenase
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(inhibitors, as auxiliary therapeutic agents; prokinetic phosphodiesterase-4 inhibitor agents for treating gastric hypomotility and related disorders)

IT 9001-66-5, Monoamine oxidase
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(inhibitors, pharmaceutical containing phosphodiesterase-4 inhibitor and; prokinetic phosphodiesterase-4 inhibitor agents for treating gastric hypomotility and related disorders)

IT 9036-21-9, Phosphodiesterase-4
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(inhibitors; prokinetic phosphodiesterase-4 inhibitor agents for treating gastric hypomotility and related disorders)

IT 52-53-9, Verapamil 525-66-6, Propranolol 4205-90-7, Clonidine 7439-89-6, Iron, biological studies 7439-92-1, Lead, biological studies 7439-93-2, Lithium, biological studies 7727-43-7, Barium sulfate 9003-53-6D, Polystyrene, resins 83150-76-9, Octreotide
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pharmaceutical containing phosphodiesterase-4 inhibitor and; prokinetic phosphodiesterase-4 inhibitor agents for treating gastric hypomotility and related disorders)

IT 52-53-9, Verapamil 525-66-6, Propranolol 4205-90-7, Clonidine 7439-89-6, Iron, biological studies 7439-92-1, Lead, biological studies 7439-93-2, Lithium, biological studies 7727-43-7, Barium sulfate 9003-53-6D, Polystyrene, resins 83150-76-9, Octreotide
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pharmaceutical containing phosphodiesterase-4 inhibitor and; prokinetic phosphodiesterase-4 inhibitor agents for treating gastric hypomotility and related disorders)

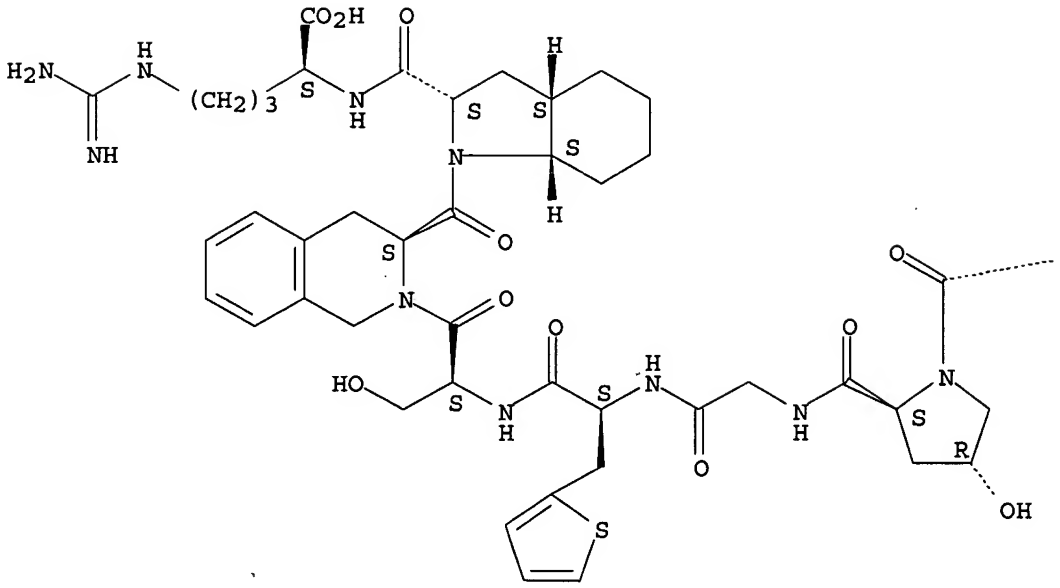
IT **603969-58-0**
RL: PAC (Pharmacological activity); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(as auxiliary therapeutic agent; prokinetic phosphodiesterase-4 inhibitor agents for treating gastric hypomotility and related disorders)

RN 603969-58-0 HCAPLUS

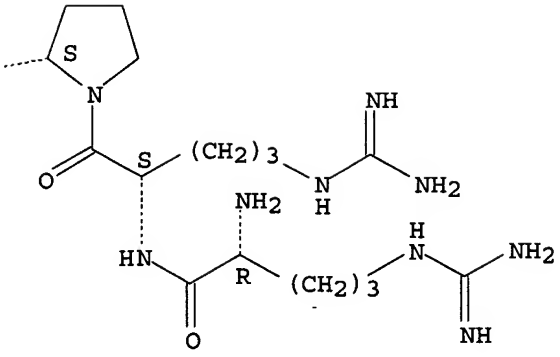
CN L-Arginine, D-arginyl-L-arginyl-L-prolyl-(4R)-4-hydroxy-L-prolylglycyl-3-(2-thienyl)-L-alanyl-L-seryl-(3S)-1,2,3,4-tetrahydro-3-isoquinolinecarbonyl-(2S,3aS,7aS)-octahydro-1H-indole-2-carbonyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



L29 ANSWER 4 OF 21 HCAPLUS COPYRIGHT 2005 ACS on STN
AN 2000:894111 HCAPLUS
DN 134:163320
ED Entered STN: 21 Dec 2000
TI Ala scan analogues of HOE 140. Synthesis and biological activities
AU Quartara, Laura; Ricci, Renzo; Meini, Stefania; Patacchini, Riccardo; Giolitti, Alessandro; Amadesi, Silvia; Rizzi, Caterina; Rizzi, Anna; Varani, Katia; Borea, Pier A.; Maggi, Carlo A.; Regoli, Domenico
CS Chemistry and Pharmacology Departments, Menarini Ricerche, Florence,

I-50131, Italy
SO European Journal of Medicinal Chemistry (2000), 35(11), 1001-1010
CODEN: EJMCA5; ISSN: 0223-5234
PB Editions Scientifiques et Medicales Elsevier
DT Journal
LA English
CC 34-3 (Amino Acids, Peptides, and Proteins)
Section cross-reference(s): 7
OS CASREACT 134:163320
AB The role of the amino acids contained in the sequence of HOE 140 (H-DArg1-Arg2-Pro3-Hyp4-Gly5-Thi6-Ser7-DTic8-Oic9-Arg10-OH), a potent and selective bradykinin B2 receptor peptide antagonist, has been investigated by the replacement of each original residue (one by one) with Ala. The resulting set of decapeptides has been tested for the B2 antagonist activity as well as for competition with the binding of [3H]BK to plasma membranes of the human umbilical vein (hUV). Pos. correlations have been established between data obtained with the bioassay and with the binding in the hUV (same species, same tissue) and also between the two bioassays, the guinea-pig ileum (GPI) and the hUV (different species, different tissue). The structure-activity study has shown that the replacement of any of the residues that constitute HOE 140 with Ala is accompanied by a decrease of potency of at least 1 log unit. The analogs can be divided into three groups, with Ala1 and Ala7 showing affinities lower than HOE 140 by a factor of 10, Ala4 and Ala10 by a factor of 100 and Ala2, Ala5, Ala6, Ala8 and Ala9 by a factor higher than 100 (100-1000). To verify the effect of chirality, the DAla5 and DSer7 analogs were synthesized and it was found that the substitution with a D-residue in position 5 is not tolerated while that in position 7 is favorable. The DSer7 derivative is the most potent analog found in this study: it shows potency as high as that of HOE 140 in the bioassays.
ST HOE 140 analog prepn bradykinin B2 receptor antagonist MSBAR
IT Enzyme kinetics
(of inhibition; preparation of HOE 140 analogs and evaluation of their biol. activities)
IT Peptides, preparation
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation of HOE 140 analogs and evaluation of their biol. activities)
IT Structure-activity relationship
(preparation of HOE 140 analogs and evaluation of their biol. activities with bradykinin B2 receptor)
IT Receptors
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(preparation of HOE 140 analogs and evaluation of their biol. activities with bradykinin B2 receptor)
IT 185145-93-1P **185145-94-2P 193618-64-3P** 324760-25-0P
324760-26-1P 324760-27-2P 324760-28-3P 324760-29-4P 324760-30-7P
324760-31-8P 324760-32-9P 324760-33-0P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation of HOE 140 analogs and evaluation of their biol. activities)
IT 185145-93-1P **185145-94-2P 193618-64-3P** 324760-25-0P
324760-26-1P 324760-27-2P 324760-28-3P 324760-29-4P 324760-30-7P
324760-31-8P 324760-32-9P 324760-33-0P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological

study); PREP (Preparation)
(preparation of HOE 140 analogs and evaluation of their biol. activities)
RE.CNT 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS RECORD
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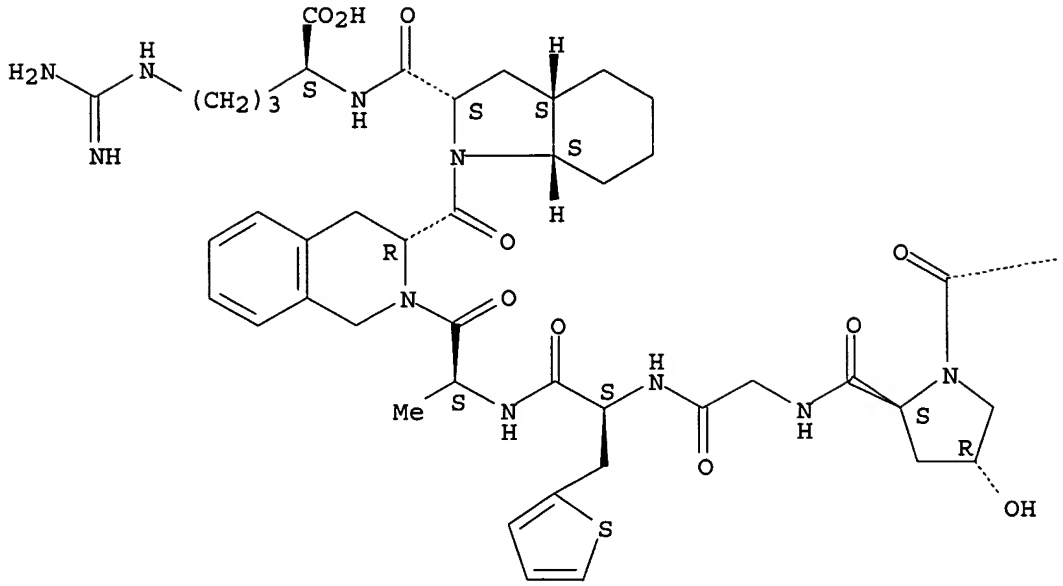
(34) Vavrek, R; Peptides 1985, V6, P161 HCAPLUS
IT **185145-94-2P 193618-64-3P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation of HOE 140 analogs and evaluation of their biol. activities)
RN 185145-94-2 HCAPLUS
CN L-Arginine, D-arginyl-L-arginyl-L-prolyl-(4R)-4-hydroxy-L-prolylglycyl-3-(2-thienyl)-L-alanyl-L-alanyl-(3R)-1,2,3,4-tetrahydro-3-isoquinolinecarbonyl-(2S,3aS,7aS)-octahydro-1H-indole-2-carbonyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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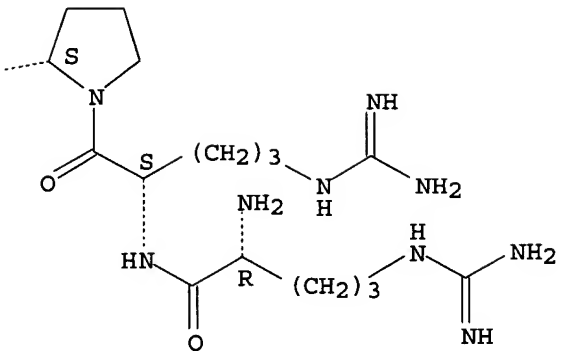
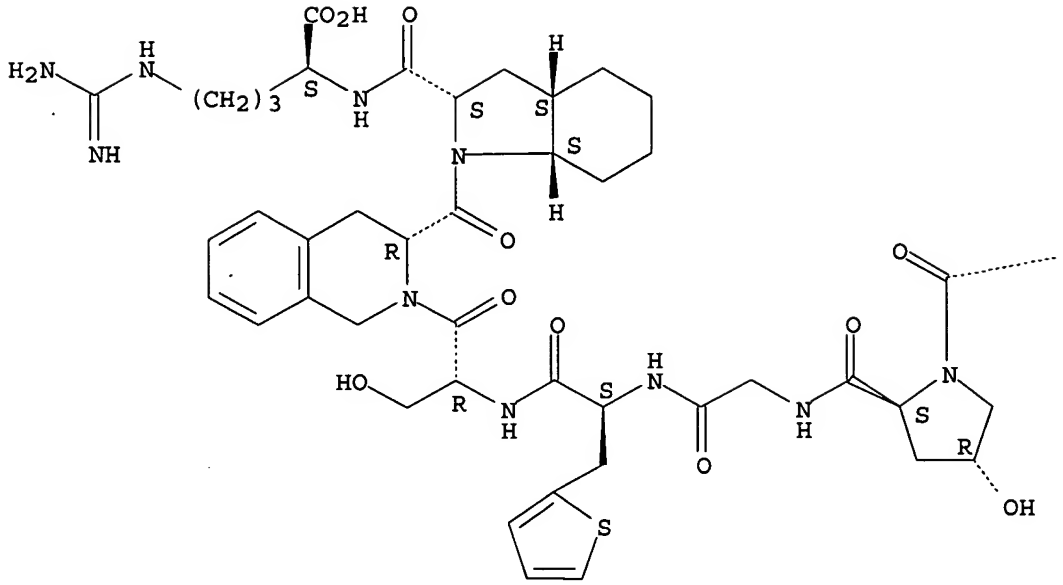


RN 193618-64-3 HCAPLUS
CN L-Arginine, D-arginyl-L-arginyl-L-prolyl-(4R)-4-hydroxy-L-prolylglycyl-3-(2-thienyl)-L-alanyl-D-seryl-(3R)-1,2,3,4-tetrahydro-3-isoquinolinecarbonyl-(2S,3aS,7aS)-octahydro-1H-indole-2-carbonyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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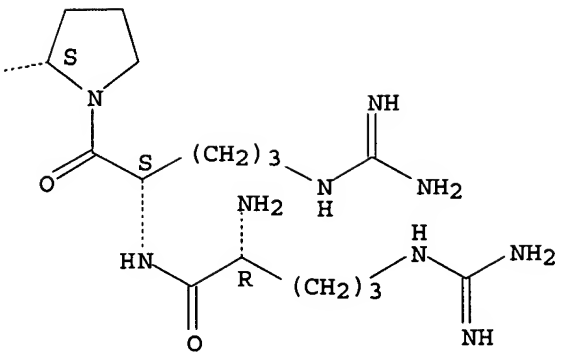


L29 ANSWER 5 OF 21 HCAPLUS COPYRIGHT 2005 ACS on STN
AN 1998:248459 HCAPLUS
DN 128:290242
ED Entered STN: 01 May 1998
TI Use of bradykinin antagonists in medications for treatment and prevention of Alzheimer's disease
IN Heitsch, Holger; Henke, Stephan; Breipohl, Gerhard; Knolle, Jochen; Wirth, Klaus; Wiemer, Gabriele

PA Hoechst A.-G., Germany
SO Ger. Offen., 8 pp.
CODEN: GWXXBX
DT Patent
LA German
IC ICM A61K038-08
CC 1-11 (Pharmacology)
Section cross-reference(s): 2
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
PI	DE 19642289	A1	19980416	DE 1996-19642289	19961014	<--
	EP 836853	A1	19980422	EP 1997-117540	19971010	<--
	EP 836853	B1	20030108			
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI					
	AT 230608	E	20030115	AT 1997-117540	19971010	<--
	ES 2190499	T3	20030801	ES 1997-117540	19971010	<--
	JP 10130163	A2	19980519	JP 1997-278301	19971013	<--
	US 6245736	B1	20010612	US 1997-949496	19971014	<--
PRAI	DE 1996-19642289	A	19961014	<--		

CLASS

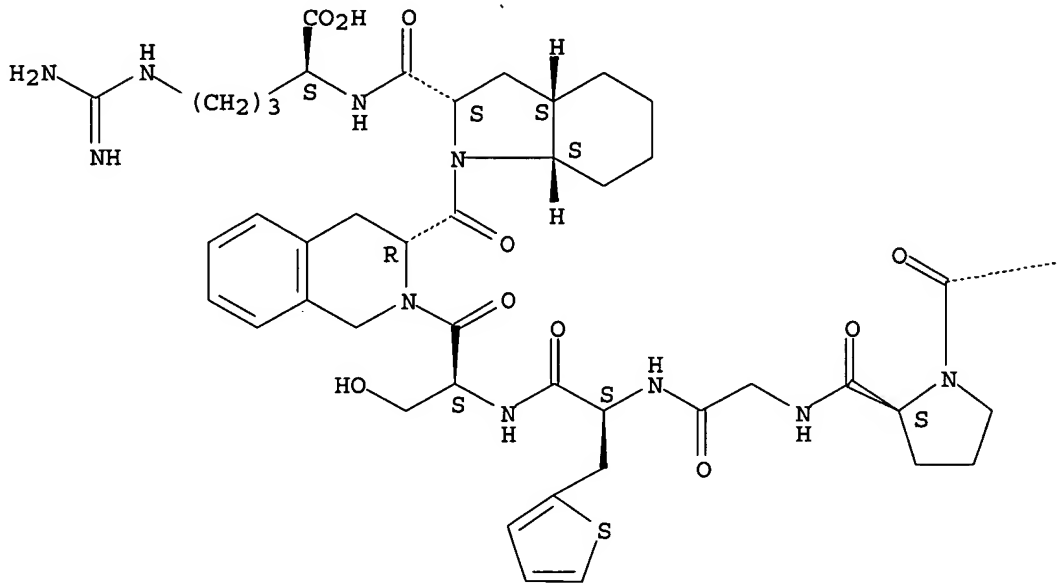
PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES	
DE 19642289	ICM	A61K038-08	
EP 836853	ECLA	A61K038/04E; C07K007/18	<--
US 6245736	NCL	514/002.000; 514/015.000; 530/314.000	
	ECLA	A61K038/04E; C07K007/18	<--

OS MARPAT 128:290242
AB Peptides with known activity as bradykinin antagonists are useful for preventing the initiation and inhibiting the progression of Alzheimer's disease and treating its symptoms. Thus, bradykinin receptor antagonists (Markush formula given) at 10-1000 nM inhibited the β/A4-amyloid-induced stimulation of cGMP production by bovine aortic and coronary endothelial cell cultures.
ST Alzheimer disease treatment bradykinin antagonist; peptide Alzheimer disease treatment
IT Anti-Alzheimer's agents
(use of bradykinin antagonists for treatment and prevention of Alzheimer's disease)
IT 58-82-2, Bradykinin
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(antagonists; use of bradykinin antagonists for treatment and prevention of Alzheimer's disease)
IT **130308-49-5 130334-55-3** 138614-30-9, HOE 140
147267-10-5, NPC 17731 150999-66-9 154131-85-8 154131-87-0
154131-88-1 154131-96-1 154132-00-0 154132-01-1 154172-56-2
156881-50-4 206054-56-0 206054-57-1 206054-58-2 206054-59-3
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(use of bradykinin antagonists for treatment and prevention of Alzheimer's disease)
IT **130308-49-5 130334-55-3**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(use of bradykinin antagonists for treatment and prevention of Alzheimer's disease)
RN 130308-49-5 HCAPLUS

CN L-Arginine, D-arginyl-L-arginyl-L-prolyl-L-prolylglycyl-3-(2-thienyl)-L-alanyl-L-seryl-(3R)-1,2,3,4-tetrahydro-3-isoquinolinecarbonyl-(2S,3aS,7aS)-octahydro-1H-indole-2-carbonyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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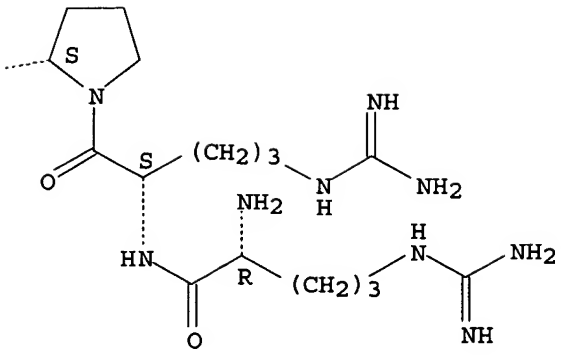
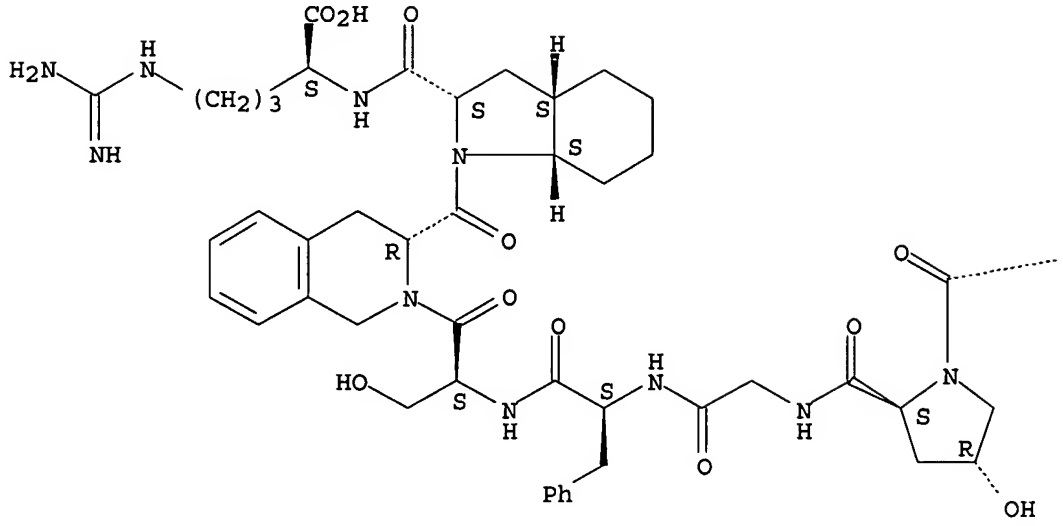


RN 130334-55-3 HCAPLUS
CN Bradykinin, N2-D-arginyl-3-(trans-4-hydroxy-L-proline)-7-(D-1,2,3,4-tetrahydro-3-isoquinolinecarboxylic acid)-8-[L-(2α,3aβ,7aβ)-octahydro-1H-indole-2-carboxylic acid]- (9CI)

(CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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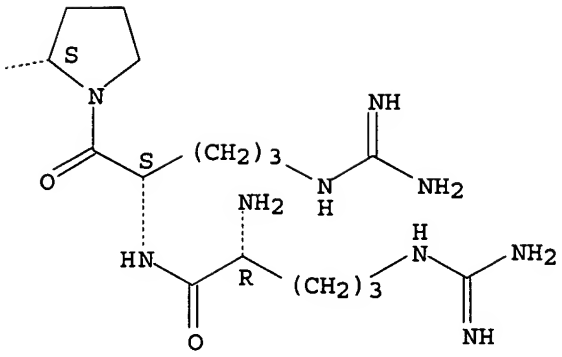


L29 ANSWER 6 OF 21 HCAPLUS COPYRIGHT 2005 ACS on STN
AN 1997:655400 HCAPLUS
DN 127:314823
ED Entered STN: 15 Oct 1997
TI Use of bradykinin antagonists for treatment of chronic fibrogenic liver diseases
IN Breipohl, Gerhard; Henke, Stephan; Knolle, Jochen; Wirth, Klausm; Hropot,

. Max; Bickel, Martin
PA Hoechst A.-G., Germany; Aventis Pharma Deutschland GmbH
SO Eur. Pat. Appl., 12 pp.
CODEN: EPXXDW
DT Patent
LA German
IC ICM A61K038-08
CC 1-9 (Pharmacology)
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
PI EP 797997	A2	19971001	EP 1997-104345	19970314	<--
EP 797997	A3	20000531			
EP 797997	B1	20050615			
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, SI, FI					
DE 19612067	A1	19971002	DE 1996-19612067	19960327	<--
US 5863901	A	19990126	US 1997-810012	19970304	<--
CA 2200040	AA	19970927	CA 1997-2200040	19970314	<--
AT 297749	E	20050715	AT 1997-104345	19970314	<--
BR 9701455	A	19980818	BR 1997-1455	19970324	<--
AU 9716516	A1	19971002	AU 1997-16516	19970325	<--
CN 1164421	A	19971112	CN 1997-104542	19970325	<--
NO 9701453	A	19970929	NO 1997-1453	19970326	<--
ZA 9702599	A	19970929	ZA 1997-2599	19970326	<--
JP 10017491	A2	19980120	JP 1997-72938	19970326	<--
PRAI DE 1996-19612067	A	19960327	<--		

CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES	
EP 797997	ICM	A61K038-08	
EP 797997	ECLA	A61K038/04E	<--
DE 19612067	ECLA	A61K038/04E	<--
US 5863901	NCL	514/015.000; 514/016.000; 514/893.000; 530/314.000; 530/327.000; 530/328.000	
	ECLA	A61K038/04E	<--
AT 297749	ECLA	A61K038/04E	<--

OS MARPAT 127:314823
AB Peptide and peptidomimetic bradykinin antagonists are useful for treatment of hepatic cirrhosis and fibrosis as well as acute liver disorders. They are also useful for prevention and treatment of complications of these diseases, e.g. portal hypertension, ascites, edema, hepatorenal syndrome, hypertensive gastropathy and colonopathy, splenomegaly, and circulatory complications. Thus, administration of HOE 140 (0.3 mg/kg s.c., twice over 6 h) to rats with CCl4-induced hepatic fibrosis reversed the Na+ retention associated with peripheral vasodilatation, edema, and ascites.
ST liver fibrosis cirrhosis bradykinin antagonist
IT Liver, disease
(fibrosis; use of bradykinin antagonists for treatment of chronic fibrogenic liver diseases)
IT Cirrhosis
Diuresis
Liver, disease
(use of bradykinin antagonists for treatment of chronic fibrogenic liver diseases)
IT Peptides, biological studies
Peptidomimetics
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(use of bradykinin antagonists for treatment of chronic fibrogenic liver diseases)

IT 58-82-2, Bradykinin
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(antagonists; use of bradykinin antagonists for treatment of chronic fibrogenic liver diseases)

IT 7440-23-5, Sodium, biological studies
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(secretion of, by kidney; use of bradykinin antagonists for treatment of chronic fibrogenic liver diseases)

IT **130308-49-5** 130308-60-0 **130334-55-3** 138614-30-9, HOE 140 140695-51-8 147267-10-5 154131-85-8 154131-88-1 154131-96-1 154132-00-0 154132-01-1 154172-56-2 156881-50-4 197370-27-7 197370-28-8 197370-29-9 197795-47-4
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(use of bradykinin antagonists for treatment of chronic fibrogenic liver diseases)

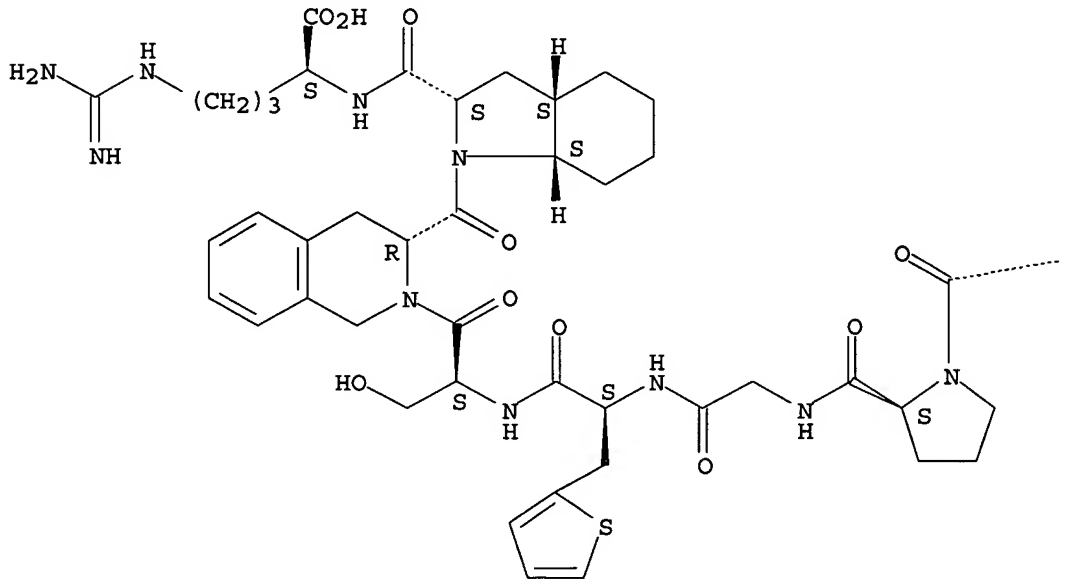
IT **130308-49-5 130334-55-3**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(use of bradykinin antagonists for treatment of chronic fibrogenic liver diseases)

RN 130308-49-5 HCAPLUS

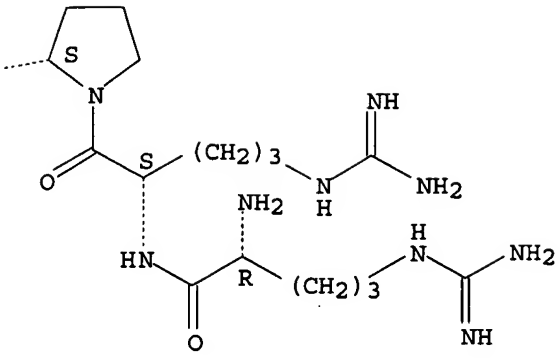
CN L-Arginine, D-arginyl-L-arginyl-L-prolyl-L-prolylglycyl-3-(2-thienyl)-L-alanyl-L-seryl-(3R)-1,2,3,4-tetrahydro-3-isoquinolinecarbonyl-(2S,3aS,7aS)-octahydro-1H-indole-2-carbonyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



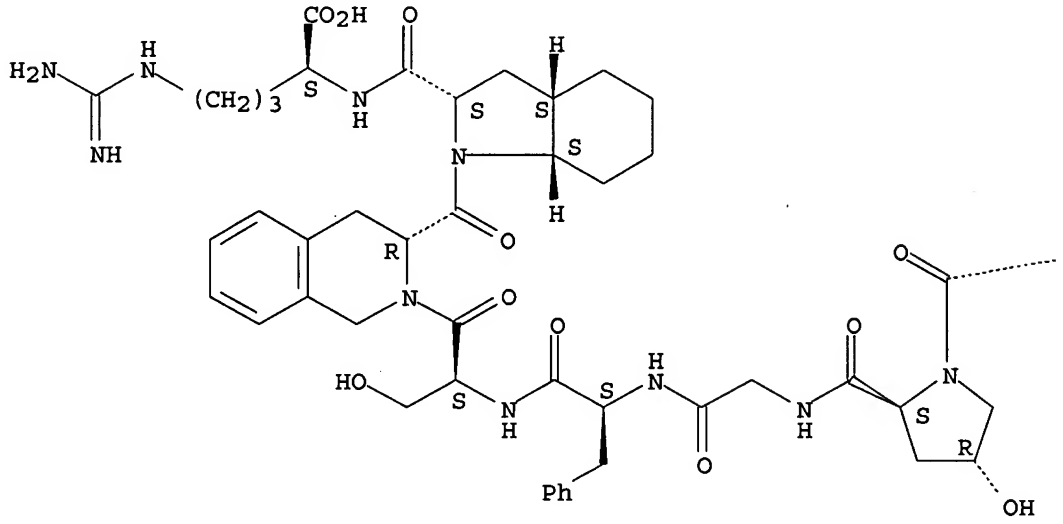
PAGE 1-B



RN 130334-55-3 HCAPLUS
CN Bradykinin, N2-D-arginyl-3-(trans-4-hydroxy-L-proline)-7-(D-1,2,3,4-tetrahydro-3-isoquinolinecarboxylic acid)-8-[L-(2α,3aβ,7aβ)-octahydro-1H-indole-2-carboxylic acid]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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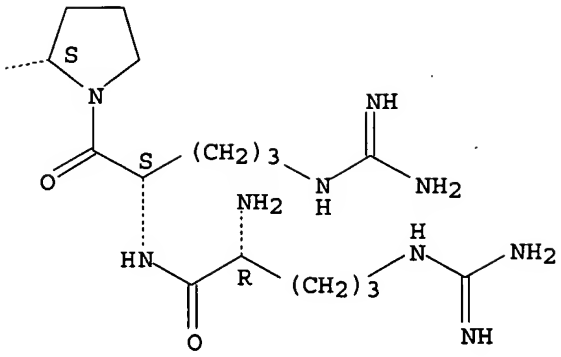

L29 ANSWER 7 OF 21 HCAPLUS COPYRIGHT 2005 ACS on STN
AN 1997:475133 HCAPLUS
DN 127:162123
ED Entered STN: 30 Jul 1997
TI Peptides having bradykinin antagonist action
IN Henke, Stephan; Anagnostopulos, Hiristo; Breipohl, Gerhard; Knolle, Jochen; Stechl, Jens; Scholkens, Bernward; et al.
PA Hoechst A.-G., Germany
SO U.S., 26 pp., Cont. of U.S. Ser. No. 236,018.
CODEN: USXXAM
DT Patent
LA English
IC ICM C07K007-18
ICS A61K038-17
INCL 514002000
CC 34-3 (Amino Acids, Peptides, and Proteins)
Section cross-reference(s): 1
FAN.CNT 4

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 5648333	A	19970715	US 1995-487442	19950607 <--
	DD 284030	A5	19901031	DD 1989-331416	19890802 <--
	ZA 8906068	A	19910130	ZA 1989-6068	19890809 <--
	DE 3926822	A1	19910221	DE 1989-3926822	19890814 <--
	DE 4013270	A1	19911031	DE 1990-4013270	19900426 <--
	RU 2083586	C1	19970710	RU 1992-5052703	19921012 <--
	LT 3375	B	19950825	LT 1993-717	19930625 <--
PRAI	DE 1988-3839581	A	19881124 <--		
	DE 1989-3916291	A	19890519 <--		
	DE 1989-3926225	A	19890603 <--		
	US 1989-374162	B2	19890630 <--		
	DE 1989-3926822	A	19890814 <--		
	DE 1990-4013270	A	19900426 <--		
	US 1990-565270	B2	19900810 <--		
	US 1991-690297	B1	19910424 <--		

US 1991-746149	B1	19910814	<--
US 1992-837090	B2	19920218	<--
US 1992-841766	B1	19920302	<--
US 1992-969523	B2	19921030	<--
US 1992-982052	B2	19921125	<--
US 1993-12849	B1	19930203	<--
US 1994-236018	A1	19940502	<--

CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
US 5648333	ICM	C07K007-18
	ICS	A61K038-17
	INCL	514002000
US 5648333	NCL	514/002.000; 514/010.000; 514/015.000; 514/803.000; 530/314.000; 530/328.000
	ECLA	C07K007/18 <--

OS MARPAT 127:162123

AB Peptides A-B-C-E-F-K-P-G-M-F [A = H, alkyl, alkanoyl, cycloalkyl, aryl, etc.; B = basic amino acid which may be substituted in side chain; C = G'-G'-Gly or G'-NH(CH2)nCO, where G' = heterocyclylcarbonyl and n = 2-8; E = aromatic amino acid radical; F, M = bond or amino acid which may be substituted in side chain; K = bond or NH(CH2)xCO, where x = 1-4; P = D-Tic (Tic = 1,2,3,4-tetrahydroisoquinolin-3-ylcarbonyl); G = bond or G'] were prepared as bradykinin antagonists. Thus, H-D-Arg-Arg-Hyp-Pro-Gly-Phe-Ser-D-Tic-Phe-Arg-OH was prepared by the solid phase method and assayed for bradykinin antagonist activity (IC50 = 4.6 x 10-6 M).

ST peptide prepn bradykinin antagonist

IT Peptides, preparation
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(peptides having bradykinin antagonist action)

IT 130308-03-1P 130308-05-3P 130308-06-4P 130308-08-6P 130308-10-0P
130308-11-1P 130308-15-5P 130308-21-3P 130308-25-7P 130308-28-0P
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130308-49-5P 130308-54-2P 130308-58-6P 130308-59-7P
130308-60-0P 130308-61-1P 130308-62-2P 130308-63-3P 130308-64-4P
130309-27-2P 130309-30-7P **130334-55-3P** 130404-60-3P
130404-96-5P **133162-75-1P** 138680-92-9P 140695-51-8P
153986-61-9P 179486-09-0P 193618-41-6P 193618-42-7P 193618-50-7P
193618-51-8P 193618-53-0P 193618-54-1P 193618-55-2P 193618-56-3P
193618-57-4P 193618-58-5P **193618-59-6P** **193618-60-9P**
193618-61-0P **193618-62-1P** **193618-63-2P**
193618-64-3P 193618-65-4P 193618-66-5P 193618-67-6P
193618-68-7P 193618-69-8P 193740-37-3P 193740-38-4P
193740-39-5P 193740-58-8P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(peptides having bradykinin antagonist action)

IT 58-82-2, Bradykinin
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(peptides having bradykinin antagonist action)

IT 130308-04-2P 130308-12-2P 130308-13-3P 130308-14-4P 130308-16-6P
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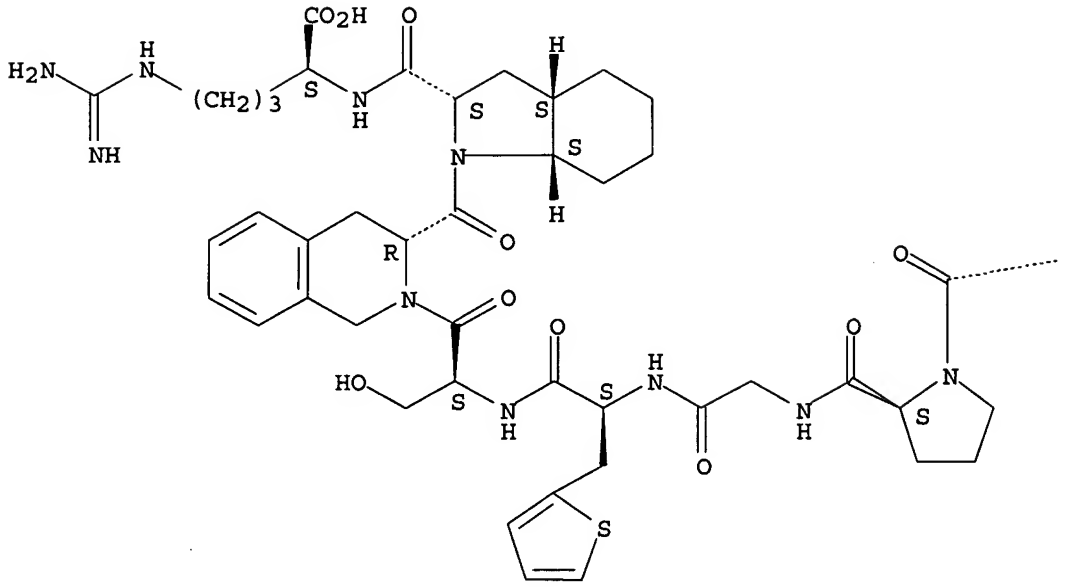
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(peptides having bradykinin antagonist action)

IT **130308-49-5P 130334-55-3P 130404-96-5P**
133162-75-1P 193618-59-6P 193618-60-9P
193618-61-0P 193618-62-1P 193618-63-2P
193618-64-3P 193618-68-7P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(peptides having bradykinin antagonist action)

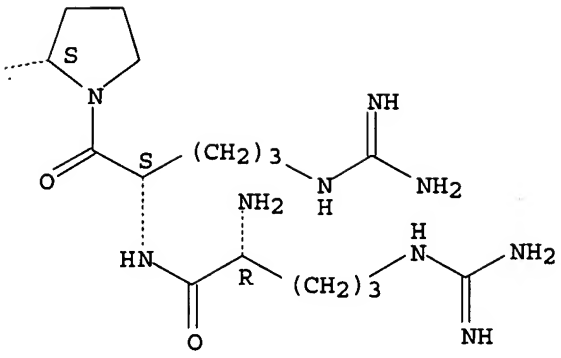
RN 130308-49-5 HCAPLUS
CN L-Arginine, D-arginyl-L-arginyl-L-prolyl-L-prolylglycyl-3-(2-thienyl)-L-alanyl-L-seryl-(3R)-1,2,3,4-tetrahydro-3-isoquinolinecarbonyl-(2S,3aS,7aS)-octahydro-1H-indole-2-carbonyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



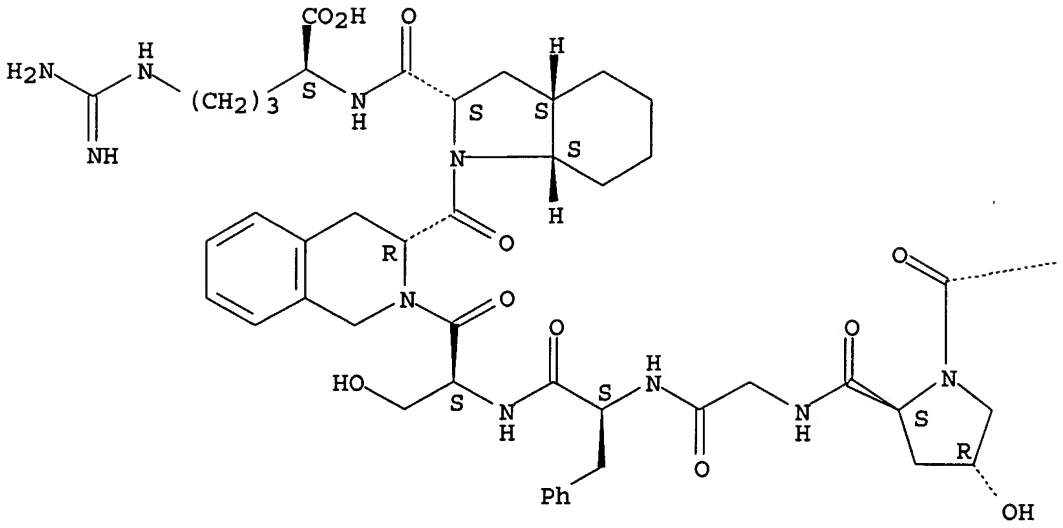
PAGE 1-B



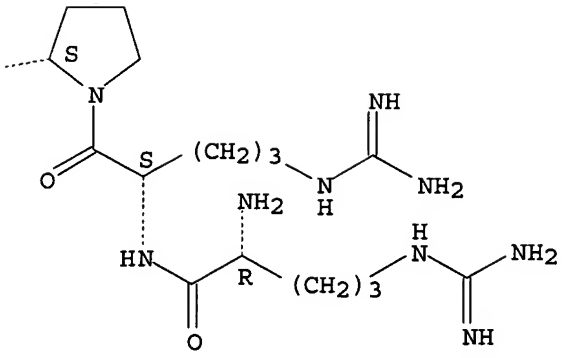
RN 130334-55-3 HCAPLUS
CN Bradykinin, N2-D-arginyl-3-(trans-4-hydroxy-L-proline)-7-(D-1,2,3,4-tetrahydro-3-isoquinolinecarboxylic acid)-8-[L-(2α,3aβ,7aβ)-octahydro-1H-indole-2-carboxylic acid]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



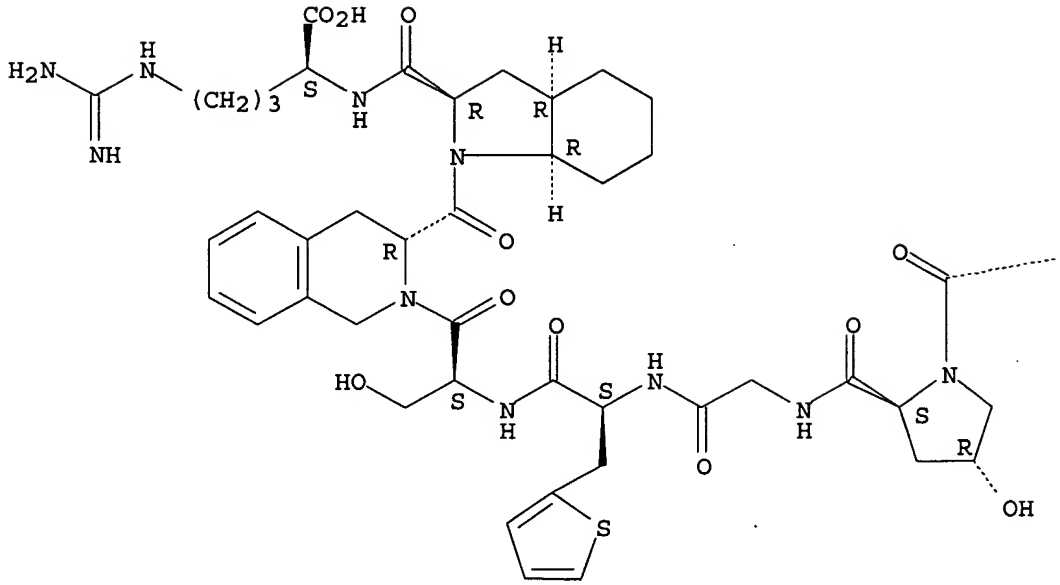
PAGE 1-B



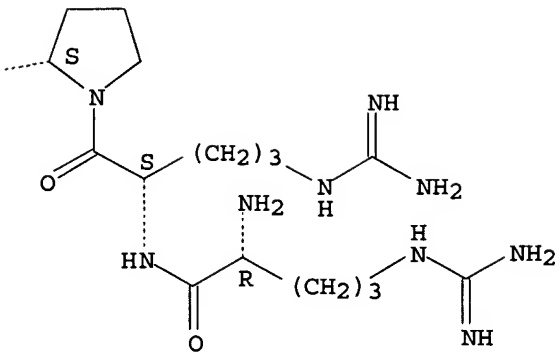
RN 130404-96-5 HCAPLUS
CN L-Arginine, D-arginyl-L-arginyl-L-prolyl-(4R)-4-hydroxy-L-prolylglycyl-3-(2-thienyl)-L-alanyl-L-seryl-(3R)-1,2,3,4-tetrahydro-3-isoquinolinecarbonyl-(2R,3aR,7aR)-octahydro-1H-indole-2-carbonyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



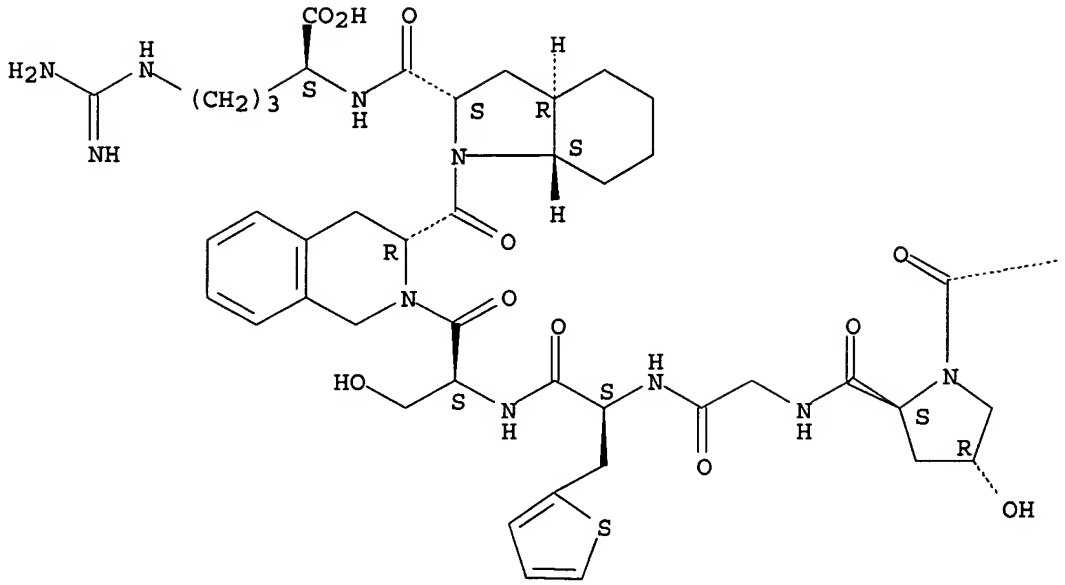
PAGE 1-B



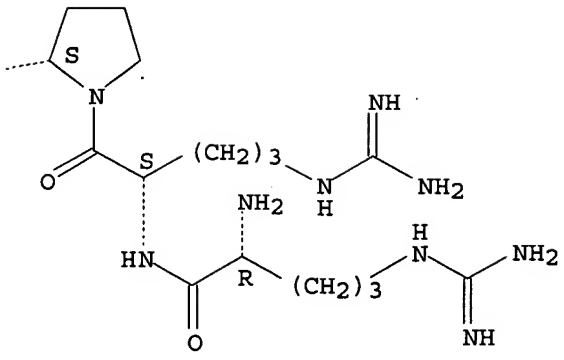
RN 133162-75-1 HCAPLUS
CN L-Arginine, D-arginyl-L-arginyl-L-prolyl-(4R)-4-hydroxy-L-prolylglycyl-3-(2-thienyl)-L-alanyl-L-seryl-(3R)-1,2,3,4-tetrahydro-3-isoquinolinecarbonyl-(2S,3aR,7aS)-octahydro-1H-indole-2-carbonyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



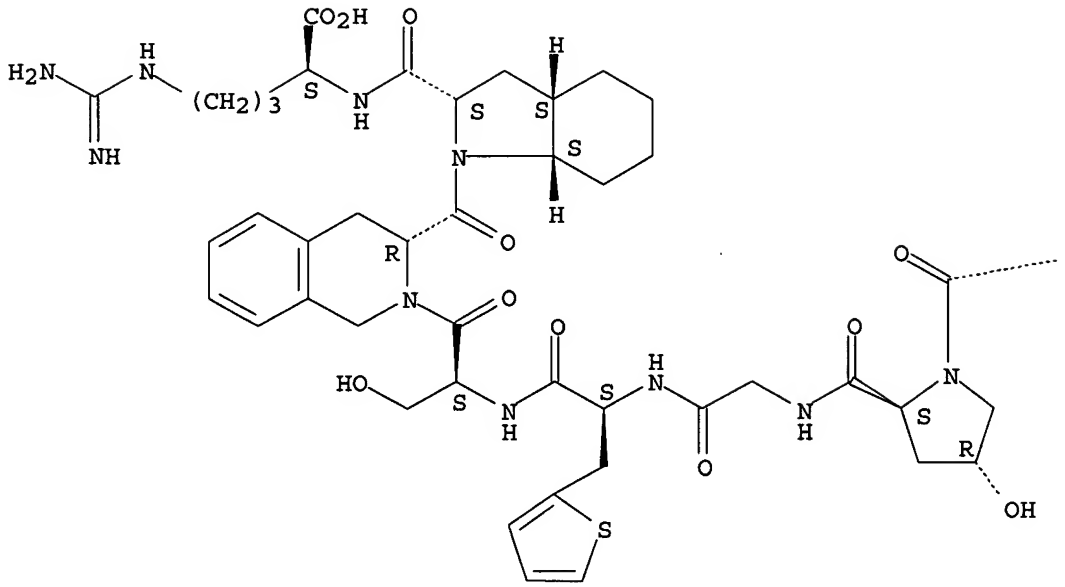
PAGE 1-B



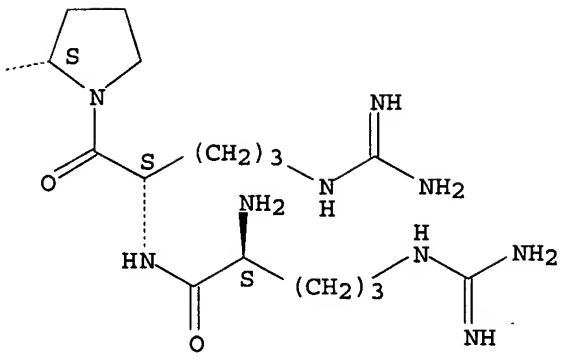
RN 193618-59-6 HCAPLUS
CN L-Arginine, L-arginyl-L-arginyl-L-prolyl-(4R)-4-hydroxy-L-prolylglycyl-3-(2-thienyl)-L-alanyl-L-seryl-(3R)-1,2,3,4-tetrahydro-3-isoquinolinecarbonyl-(2S,3aS,7aS)-octahydro-1H-indole-2-carbonyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



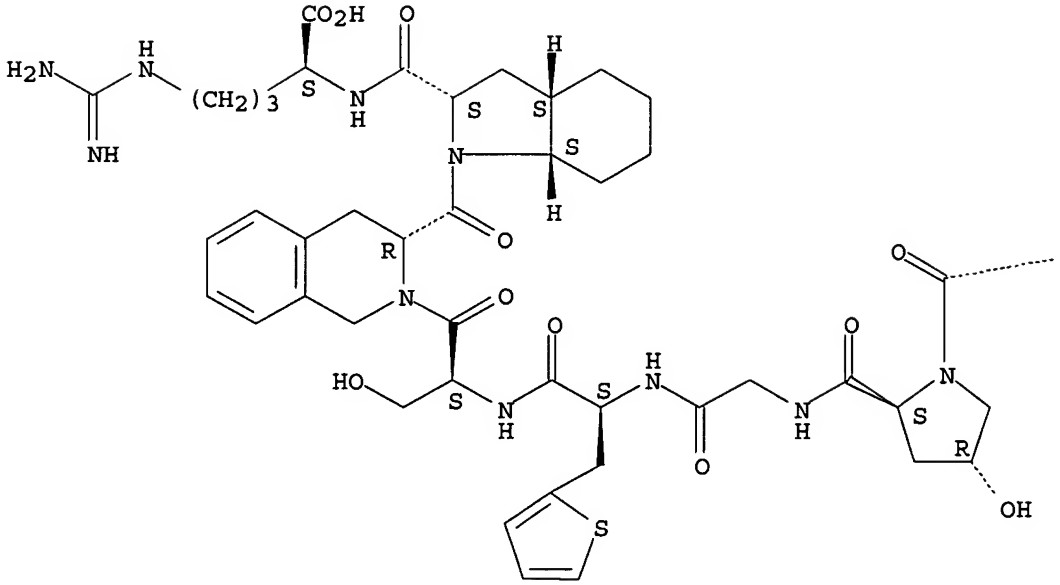
PAGE 1-B



RN 193618-60-9 HCAPLUS
CN L-Arginine, D-arginyl-D-arginyl-L-prolyl-(4R)-4-hydroxy-L-prolylglycyl-3-(2-thienyl)-L-alanyl-L-seryl-(3R)-1,2,3,4-tetrahydro-3-isoquinolinecarbonyl-(2S,3aS,7aS)-octahydro-1H-indole-2-carbonyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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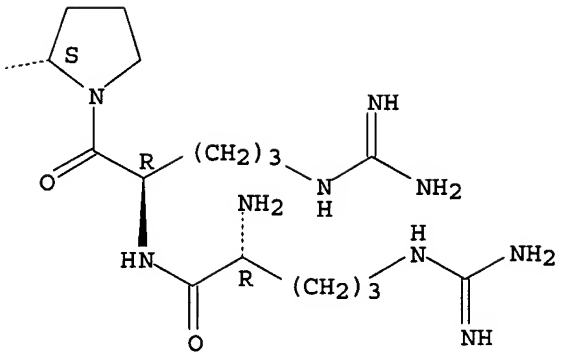
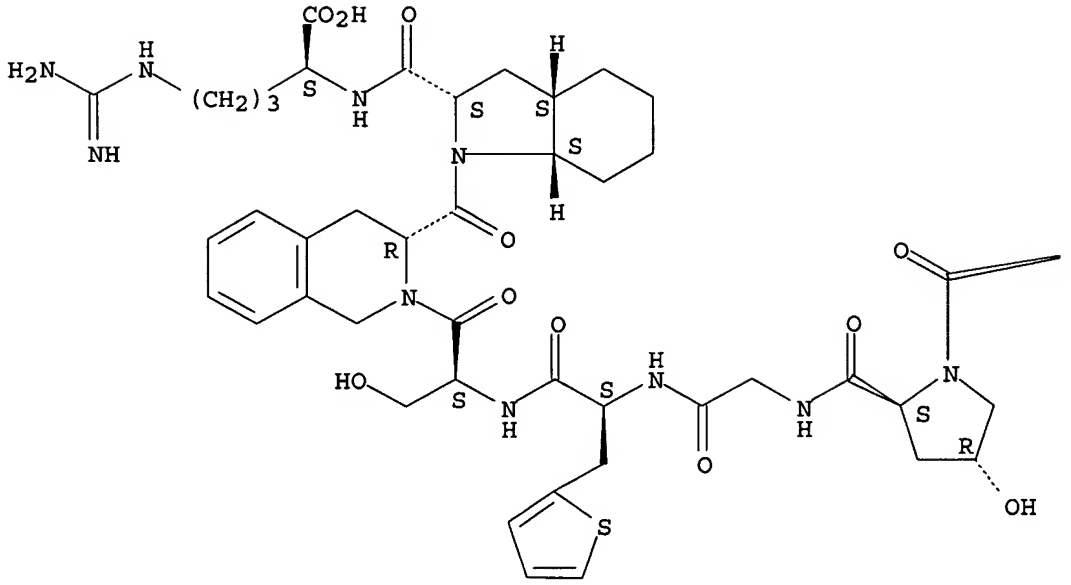


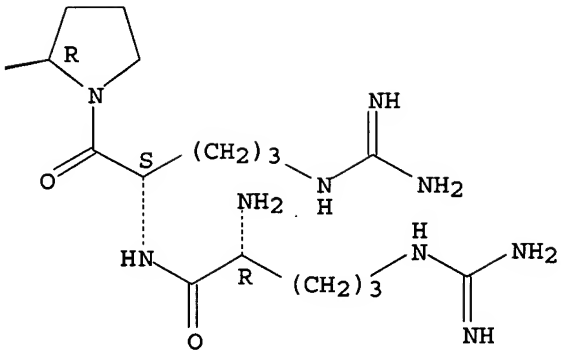
RN 193618-61-0 HCAPLUS
CN L-Arginine, D-arginyl-L-arginyl-D-prolyl-(4R)-4-hydroxy-L-prolylglycyl-3-(2-thienyl)-L-alanyl-L-seryl-(3R)-1,2,3,4-tetrahydro-3-isoquinolinecarbonyl-(2S,3aS,7aS)-octahydro-1H-indole-2-carbonyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



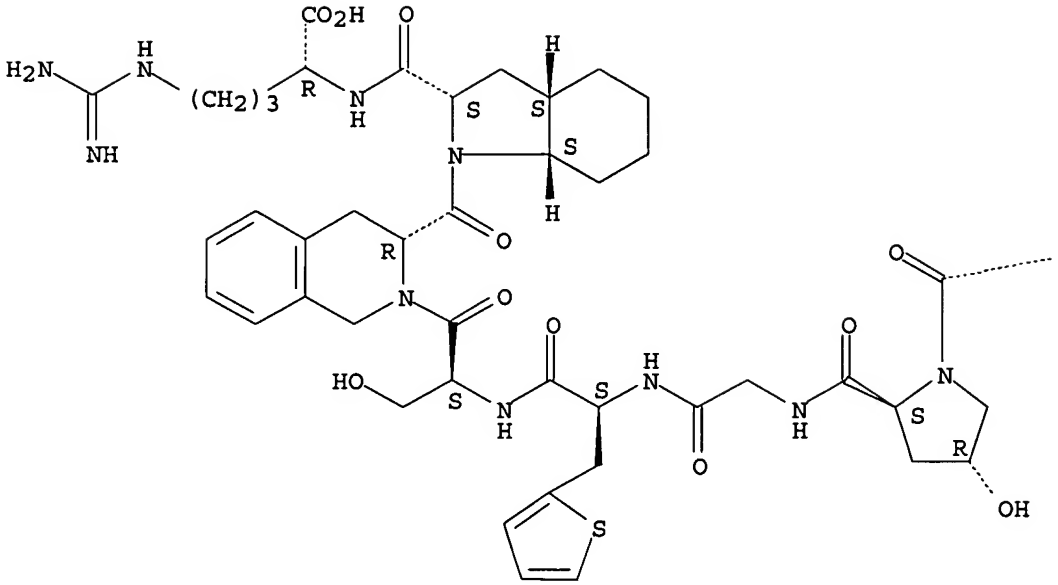
PAGE 1-B



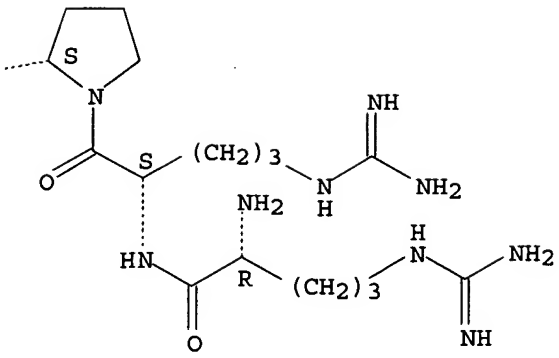
RN 193618-62-1 HCAPLUS
CN D-Arginine, D-arginyl-L-arginyl-L-prolyl-(4R)-4-hydroxy-L-prolylglycyl-3-(2-thienyl)-L-alanyl-L-seryl-(3R)-1,2,3,4-tetrahydro-3-isoquinolinecarbonyl-(2S,3aS,7aS)-octahydro-1H-indole-2-carbonyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



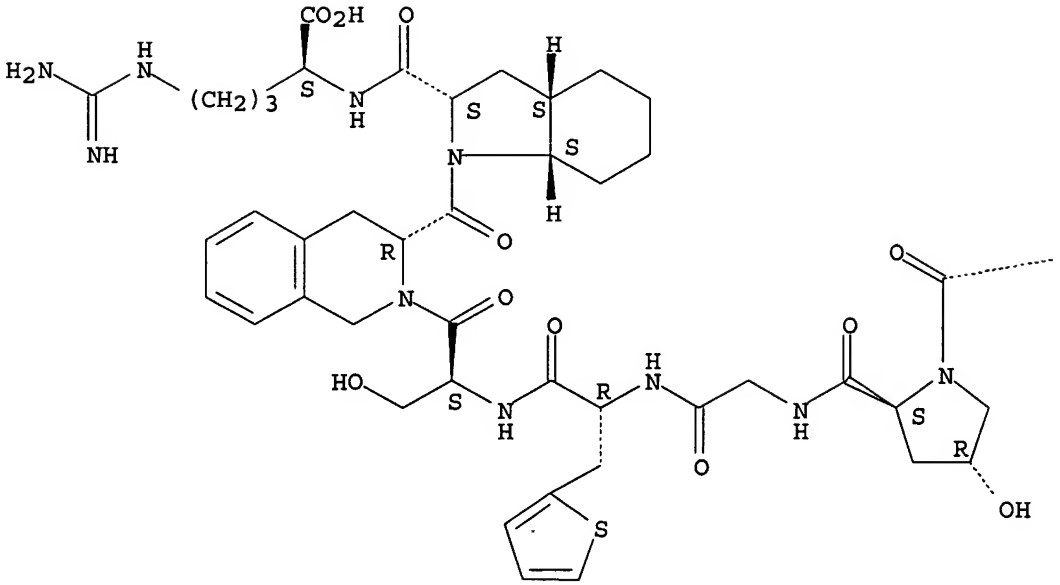
PAGE 1-B



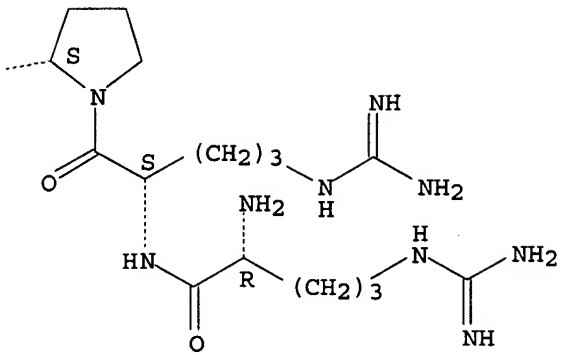
RN 193618-63-2 HCAPLUS
CN L-Arginine, D-arginyl-L-arginyl-L-prolyl-(4R)-4-hydroxy-L-prolylglycyl-3-(2-thienyl)-D-alanyl-L-seryl-(3R)-1,2,3,4-tetrahydro-3-isoquinolinecarbonyl-(2S,3aS,7aS)-octahydro-1H-indole-2-carbonyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



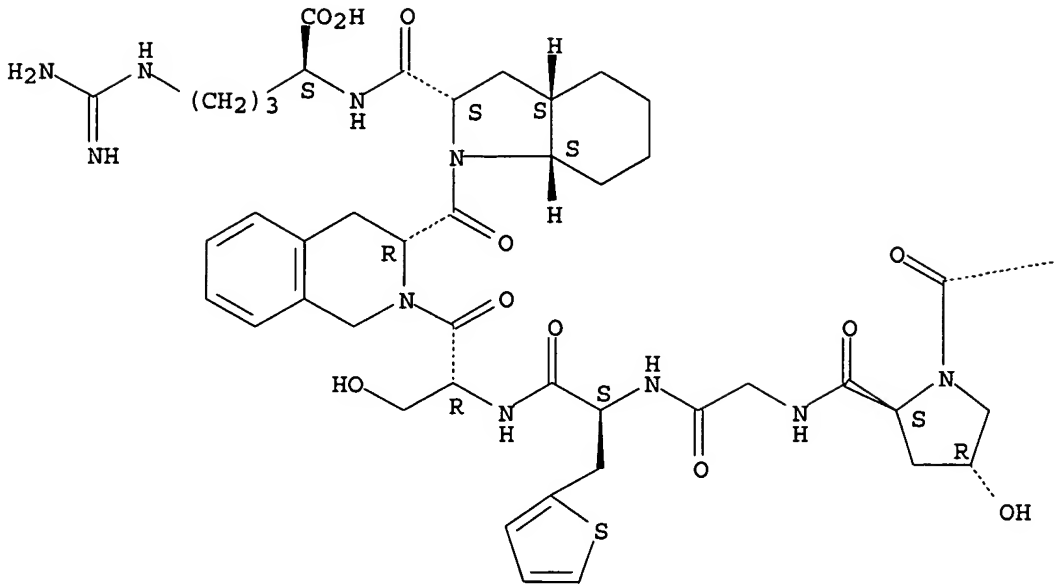
PAGE 1-B



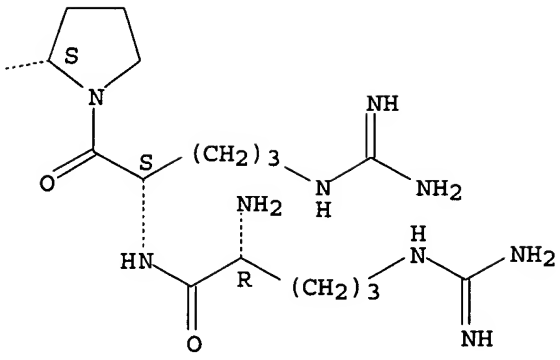
RN 193618-64-3 HCAPLUS
CN L-Arginine, D-arginyl-L-arginyl-L-prolyl-(4R)-4-hydroxy-L-prolylglycyl-3-(2-thienyl)-L-alanyl-D-seryl-(3R)-1,2,3,4-tetrahydro-3-isoquinolinecarbonyl-(2S,3aS,7aS)-octahydro-1H-indole-2-carbonyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



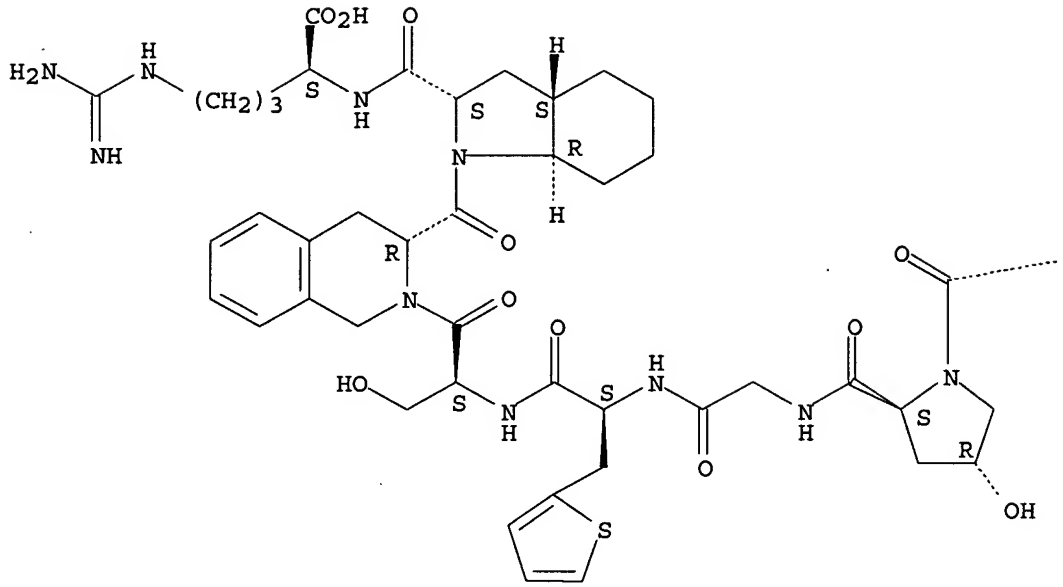
PAGE 1-B



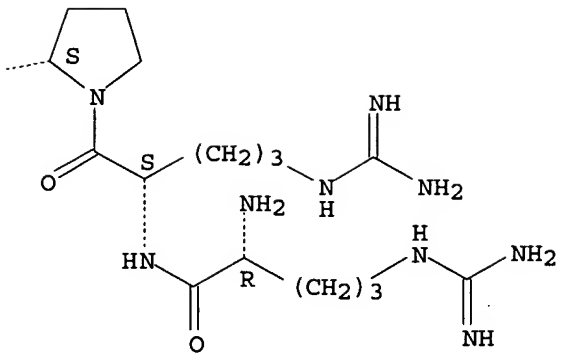
RN 193618-68-7 HCAPLUS
CN L-Arginine, D-arginyl-L-arginyl-L-prolyl-(4R)-4-hydroxy-L-prolylglycyl-3-(2-thienyl)-L-alanyl-L-seryl-(3R)-1,2,3,4-tetrahydro-3-isoquinolinecarbonyl-(2S,3aS,7aR)-octahydro-1H-indole-2-carbonyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



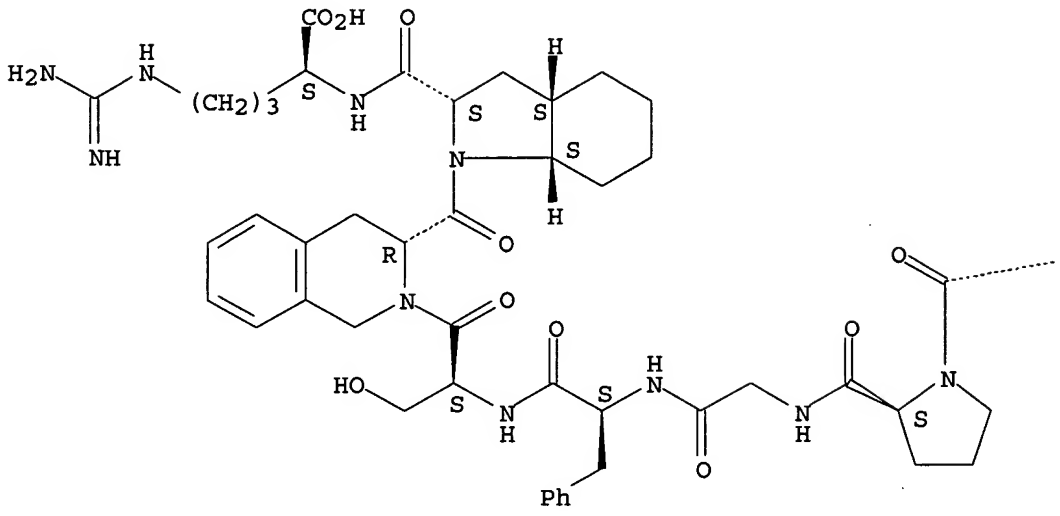
PAGE 1-B



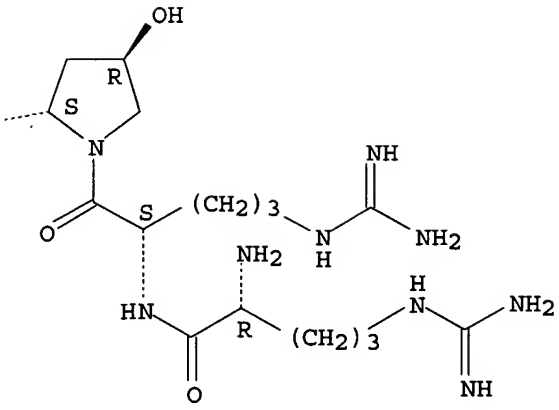
IT **130308-52-0P 130308-53-1P**
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(peptides having bradykinin antagonist action)
RN 130308-52-0 HCAPLUS
CN Bradykinin, N2-D-arginyl-2-(trans-4-hydroxy-L-proline)-7-(D-1,2,3,4-tetrahydro-3-isoquinolinecarboxylic acid)-8-[(2α,3aβ,7aβ)-L-octahydro-1H-indole-2-carboxylic acid]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



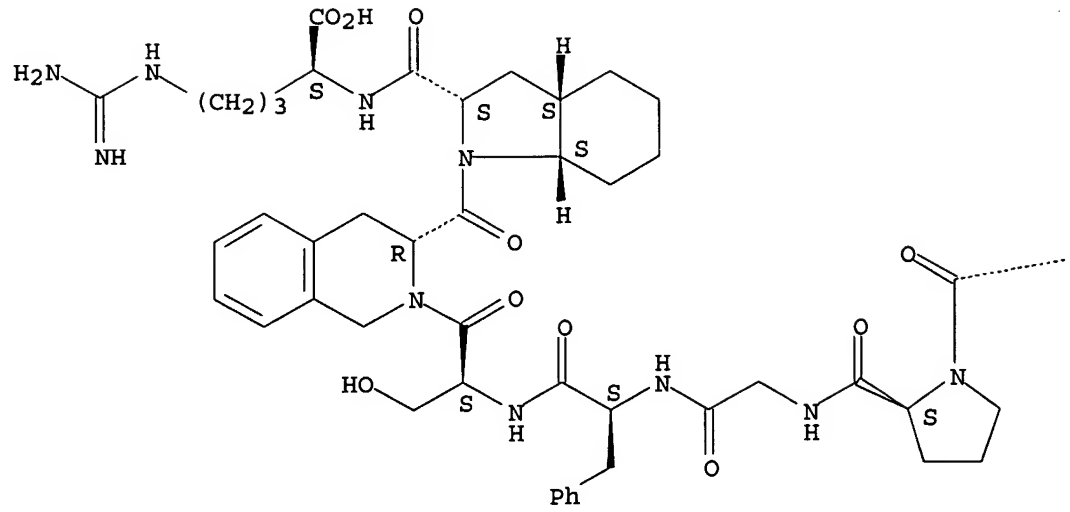
PAGE 1-B



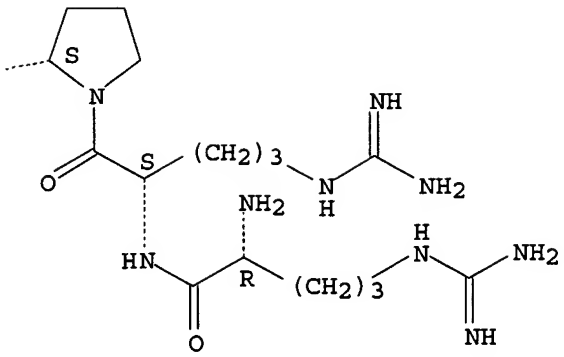
RN 130308-53-1 HCAPLUS
CN Bradykinin, N2-D-arginyl-7-(D-1,2,3,4-tetrahydro-3-isoquinolinecarboxylic acid)-8-[(2α,3aβ,7aβ)-L-octahydro-1H-indole-2-carboxylic acid]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B

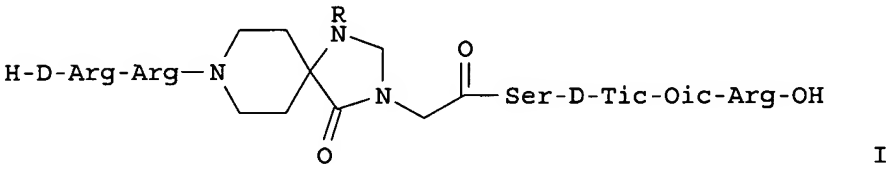


L29 ANSWER 8 OF 21 HCAPLUS COPYRIGHT 2005 ACS on STN
AN 1996:681794 HCAPLUS
DN 126:54996
ED Entered STN: 20 Nov 1996
TI Mutations in the B2 bradykinin receptor reveal a different pattern of contacts for peptidic agonists and peptidic antagonists
AU Jarnagin, Kurt; Bhakta, Sunil; Zuppan, Patty; Yee, Calvin; Ho, Teresa; Phan, Thu; Tahilramani, Ram; Pease, Joe H. B.; Miller, Aaron; Freedman, Richard
CS Molecular Pharmacology, Roche Bioscience, Palo Alto, CA, 94304, USA
SO Journal of Biological Chemistry (**1996**), 271(45), 28277-28286

CODEN: JBCHA3; ISSN: 0021-9258
PB American Society for Biochemistry and Molecular Biology
DT Journal
LA English
CC 2-2 (Mammalian Hormones)
AB The B2 bradykinin receptor, a seven-helix transmembrane receptor, binds the inflammatory mediator bradykinin (BK) and the structurally related peptide antagonist HOE-140. The binding of HOE-140 and the binding of bradykinin are mutually exclusive and competitive. Fifty-four site-specific receptor mutations were made. BK's affinity is reduced 2200-fold by F261A, 490-fold by T265A, 60-fold by D286A, and 3-10-fold by N200A, D268A, and Q290A. In contrast, HOE-140 affinity is reduced less than 7-fold by F254A, F261A, Y297A, and Q262A. The almost complete discordance of mutations that affect BK binding vs. HOE-140 binding is surprising, but it was paralleled by the effect of single changes in BK and HOE-140. [Ala9]BK and [Ala6]BK are reduced in receptor binding affinity 27,000- and 150-fold, resp., while [Ala9]HOE-140 affinity is reduced 7-fold and [Ala6]HOE-140 affinity is unchanged. NMR spectroscopy of all of the peptidic analogs of BK or HOE-140 revealed a β-turn at the C terminus. Models of the receptor-ligand complex suggested that bradykinin is bound partially inside the helical bundle of the receptor with the amino terminus emerging from the extracellular side of helical bundle. In these models a salt bridge occurs between Arg9 and Asp286; the models also place Phe8 in a hydrophobic pocket midway through the transmembrane region. Models of HOE-140 binding to the receptor place its β-turn one α-helical turn deeper and closer to helix 7 and helix 1 as compared with bradykinin-receptor complex models.
ST bradykinin B2 receptor structure activity; HOE 140 bradykinin B2 receptor structure
IT Bradykinin receptors
RL: BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); PROC (Process)
(B2; bradykinin B2 receptor structure-activity studies reveal different pattern of contacts for peptidic agonists and peptidic antagonists)
IT Structure-activity relationship
(ligand-binding; bradykinin B2 receptor structure-activity studies reveal different pattern of contacts for peptidic agonists and peptidic antagonists)
IT Conformation
Helix (conformation)
(protein; bradykinin B2 receptor structure-activity studies reveal different pattern of contacts for peptidic agonists and peptidic antagonists)
IT Structure-activity relationship
(receptor-binding; bradykinin B2 receptor structure-activity studies reveal different pattern of contacts for peptidic agonists and peptidic antagonists)
IT 58-82-2, Bradykinin 3322-88-1, [Ala6]-bradykinin 3322-91-6 138614-30-9, HOE-140 185145-93-1 **185145-94-2**
RL: BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); PROC (Process)
(bradykinin B2 receptor structure-activity studies reveal different pattern of contacts for peptidic agonists and peptidic antagonists)

L29 ANSWER 9 OF 21 HCAPLUS COPYRIGHT 2005 ACS on STN
AN 1996:422410 HCAPLUS
DN 125:168616
ED Entered STN: 18 Jul 1996
TI Synthesis and Characterization of Pseudopeptide Bradykinin B2 Receptor Antagonists Containing the 1,3,8-Triazaspiro[4.5]decan-4-one Ring System

AU Mavunkel, Babu J.; Lu, Zhijian; Goehring, R. Richard; Lu, Songfeng; Chakravarty, Sarvajit; Perumattam, John; Novotny, Elizabeth A.; Connolly, Maureen; Valentine, Heather; Kyle, Donald J.
CS Scios Nova Inc., Sunnyvale, CA, 94086, USA
SO Journal of Medicinal Chemistry (**1996**), 39(16), 3169-3173
CODEN: JMCMAR; ISSN: 0022-2623
PB American Chemical Society
DT Journal
LA English
CC 34-3 (Amino Acids, Peptides, and Proteins)
Section cross-reference(s): 1, 2
OS CASREACT 125:168616
GI



I

AB A series of pseudopeptides I (R = Ph, 4-MeC6H4, cyclohexylmethyl, Pr, cyclohexyl, PhCH2CH2; Tic = 1,2,3,4-tetrahydroisoquinoline-3-carbonyl; Oic = octahydroindane-2-carbonyl) containing substituted 1,3,8-triazaspiro[4.5]decan-4-one-3-acetic acid residues as amino acid surrogates to replace the Pro2-Pro3-Gly4-Phe5 section of the peptide bradykinin B2 receptor antagonist [Pro3, Phe5]HOE 140 (D-Arg0-Arg1-Pro2-Pro3-Gly4-Phe5-Ser6-D-Tic7-Oic8-Arg9) were prepared Pseudopeptides I were examined in vitro for their B2 receptor affinities as well as for their ability to block bradykinin mediated actions in vivo. Two compds. in particular, NPC 18521 (I; R = Ph) and NPC 18688 (I; R = cyclohexyl) were quite potent in these latter assays, indicating that a significant portion of this prototypical second generation decapeptide antagonist can be replaced with a more compact nonpeptide mol.
ST triazaspirodecanone pseudopeptide prepn bradykinin antagonist; NPC 18521 18688 prepn bradykinin antagonist
IT Receptors
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(bradykinin B2, antagonists; preparation and characterization of pseudopeptide bradykinin B2 receptor antagonists containing a triazaspirodecanone ring system)
IT Peptides, preparation
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(pseudo-, triazaspirodecanone; preparation and characterization of pseudopeptide bradykinin B2 receptor antagonists containing a triazaspirodecanone ring system)
IT **130308-53-1DP**, analogs 168824-73-5P, NPC 18521 168824-74-6P 168824-75-7P 168824-77-9P 174693-30-2P, NPC 18688 180386-41-8P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation and characterization of pseudopeptide bradykinin B2 receptor antagonists containing a triazaspirodecanone ring system)
IT 62-53-3, Aniline, reactions 64-04-0, 2-Phenylethylamine 96-32-2,

Methyl bromoacetate 106-49-0, 4-Methylaniline, reactions 108-91-8, Cyclohexylamine, reactions 3218-02-8, Cyclohexanemethanamine 3612-20-2, 1-Benzyl-4-piperidone 13836-37-8D, resin-bound 109523-13-9
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation and characterization of pseudopeptide bradykinin B2 receptor antagonists containing a triazaspirodecanone ring system)

IT 180386-30-5P 180386-31-6P 180386-32-7P 180386-33-8P 180386-34-9P 180386-35-0P 180386-36-1P 180386-37-2P 180386-38-3P 180386-39-4P 180386-40-7P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and characterization of pseudopeptide bradykinin B2 receptor antagonists containing a triazaspirodecanone ring system)

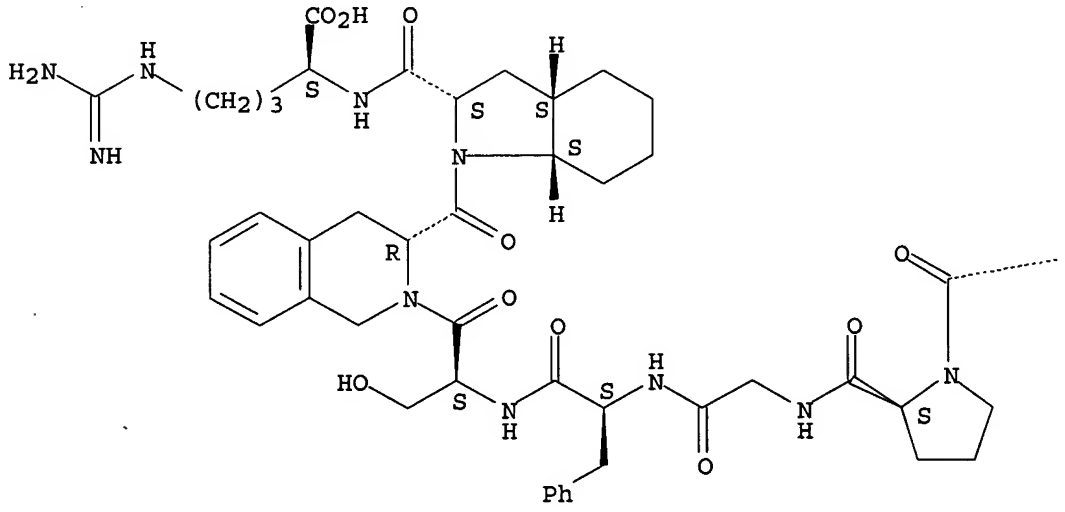
IT **130308-53-1DP**, analogs
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation and characterization of pseudopeptide bradykinin B2 receptor antagonists containing a triazaspirodecanone ring system)

RN 130308-53-1 HCAPLUS

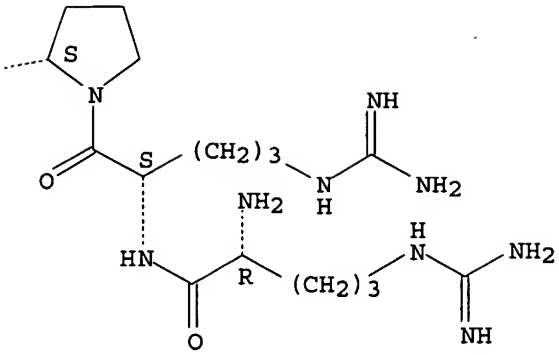
CN Bradykinin, N2-D-arginyl-7-(D-1,2,3,4-tetrahydro-3-isoquinolinecarboxylic acid)-8-[(2α,3aβ,7aβ)-L-octahydro-1H-indole-2-carboxylic acid]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



L29 ANSWER 10 OF 21 HCAPLUS COPYRIGHT 2005 ACS on STN
AN 1994:681159 HCAPLUS
DN 121:281159
ED Entered STN: 10 Dec 1994
TI A systematic study of the SAR in second generation bradykinin antagonists leads to the design of the first high affinity cyclic peptide antagonists
AU Chakravarty, S.; Mavunkel, B. J.; Lu, S.; Wilkins, D. E.; Kyle, D. J.
CS Scios Nova Inc., Baltimore, MD, 21224, USA
SO Pept.: Chem., Struct. Biol., Proc. Am. Pept. Symp., 13th (**1994**), Meeting Date 1993, 381-3. Editor(s): Hodges, Robert S.; Smith, John A. Publisher: ESCOM, Leiden, Neth.
CODEN: 60LXAW
DT Conference
LA English
CC 34-3 (Amino Acids, Peptides, and Proteins)
Section cross-reference(s): 2
AB A report from a symposium on structure-activity profiles of bradykinin antagonist peptide NPC 18545 (H-D-Arg0-Arg1-Pro2-Hyp3-Gly4-Phe5-Ser6-D-Tic7-Oic8-Arg9-OH) (Tic = 1,2,3,4-tetrahydroisoquinoline-3-carboxylic acid, Oic = octahydroindole-2-carboxylic acid) by systematic replacements of residues 1-5 with glycine.
ST bradykinin antagonist structure activity symposium; NPC 18545 structure activity symposium
IT Molecular structure-biological activity relationship
(bradykinin-inhibiting, a systematic study of the structure-activity relationships in second generation bradykinin antagonists leads to the design of the first high affinity cyclic peptide antagonists)
IT 58-82-2, Bradykinin
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(antagonists; a systematic study of the structure-activity relationships in second generation bradykinin antagonists leads to the design of the first high affinity cyclic peptide antagonists)
IT 58-82-2, Bradykinin
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL

(Biological study); PROC (Process)
(antagonists; a systematic study of the structure-activity relationships in second generation bradykinin antagonists leads to the design of the first high affinity cyclic peptide antagonists)

L29 ANSWER 11 OF 21 HCAPLUS COPYRIGHT 2005 ACS on STN
AN 1994:450783 HCAPLUS
DN 121:50783
ED Entered STN: 06 Aug 1994
TI Effects of peptide and nonpeptide antagonists of bradykinin B2 receptors on the venoconstrictor action of bradykinin
AU Marceau, Francois; Levesque, Luc; Drapeau, Guy; Rioux, Francis; Salvino, Joseph M.; Wolfe, Henry R.; Seoane, Peter R.; Sawutz, David G.
CS Centre Recherche, Hotel-Dieu de Quebec, QC, G1R 2J6, Can.
SO Journal of Pharmacology and Experimental Therapeutics (**1994**), 269(3), 1136-43
CODEN: JPETAB; ISSN: 0022-3565
DT Journal
LA English
CC 2-10 (Mammalian Hormones)
Section cross-reference(s): 1
AB The isolated rabbit jugular and human umbilical veins respond to bradykinin (BK) by contractions that are mediated by the BK B2 type receptors. In this report, the pharmacol. of recently developed BK B2 receptor antagonists is assessed by using these prepns. The nonpeptide kinin antagonist WIN 64338 demonstrates competitive and surmountable antagonism of BK in both the jugular and the umbilical veins (pA2 values of 6.14 and 5.99, resp.). WIN 64338 shows selectivity in its antagonist action as it does not inhibit the effect of various other contractile agents in either of the prepns. HOE-140, a "second generation" peptide antagonist of BK, behaves as an insurmountable and irreversible antagonist in the rabbit jugular vein, but appears to be competitive in the umbilical vein (pA2 = 8.2). In the jugular vein, [L-Tic7]HOE-140 is an insurmountable antagonist about 2000-fold less potent than HOE-140; the L-Tic7 isomer demonstrates no significant antagonist activity on the umbilical vein at 30 μM. This study confirms that WIN 64338 behaves as a competitive and selective kinin antagonist of the BK B2 type receptors. The pharmacol. profile of the L-Tic7 analog of HOE-140 may provide useful information in discerning the mol. interaction of noncompetitive BK antagonists with their receptors.
ST venoconstrictor bradykinin B2 receptor antagonist
IT Receptors
RL: BIOL (Biological study)
(bradykinin B2, antagonists of, bradykinin-induced vein constriction in response to, in human and laboratory animal)
IT Vein
(jugular, constriction of, by bradykinin, bradykinin B2 receptor antagonist effect on)
IT Vein
(umbilical, constriction of, by bradykinin in human, bradykinin B2 receptor antagonist effect on)
IT 130308-48-4, HOE-140 151039-63-3, WIN 64338 **153322-84-0**, [L-Tic7]HOE-140
RL: BIOL (Biological study)
(bradykinin-induced vein constriction inhibition by, in human and laboratory animal, receptor B2 in)
IT 130308-48-4, HOE-140 151039-63-3, WIN 64338 **153322-84-0**, [L-Tic7]HOE-140
RL: BIOL (Biological study)
(bradykinin-induced vein constriction inhibition by, in human and laboratory

animal, receptor B2 in)

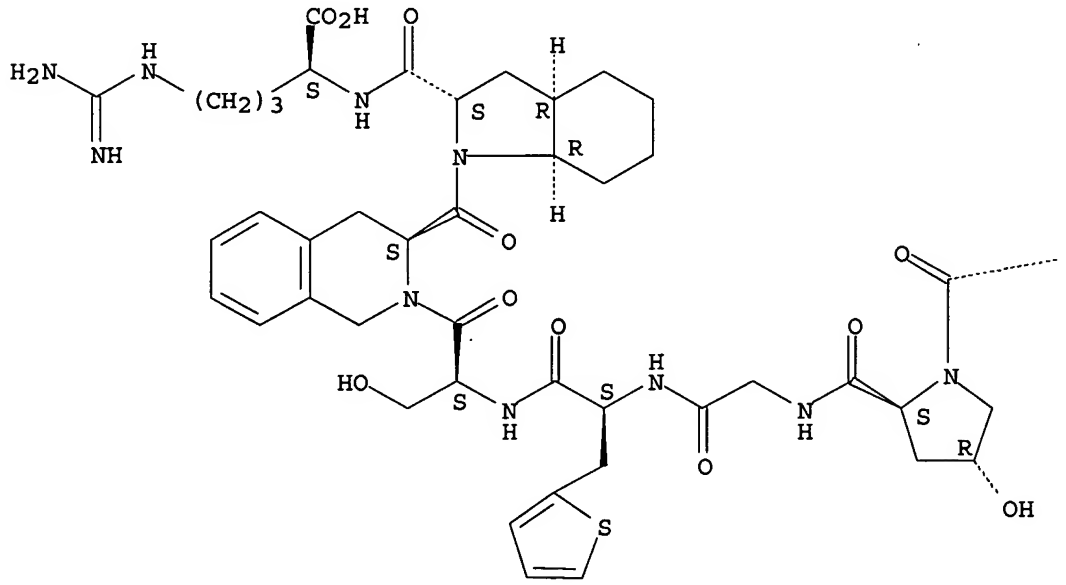
IT **153322-84-0**, [L-Tic7]HOE-140
RL: BIOL (Biological study)
(bradykinin-induced vein constriction inhibition by, in human and laboratory animal, receptor B2 in)

RN 153322-84-0 HCAPLUS

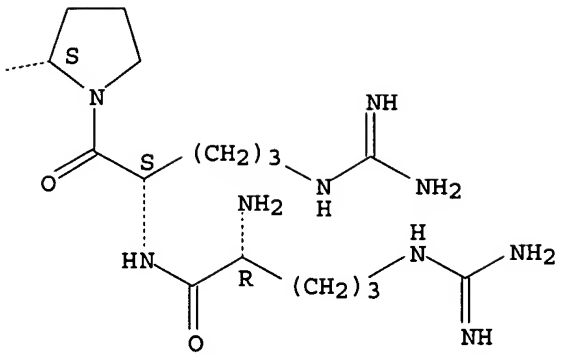
CN L-Arginine, D-arginyl-L-arginyl-L-prolyl-trans-4-hydroxy-L-prolylglycyl-3-(2-thienyl)-L-alanyl-L-seryl-L-1,2,3,4-tetrahydro-3-isoquinolinecarbonyl-L-(2α,3aβ,7aβ)-octahydro-1H-indole-2-carbonyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B

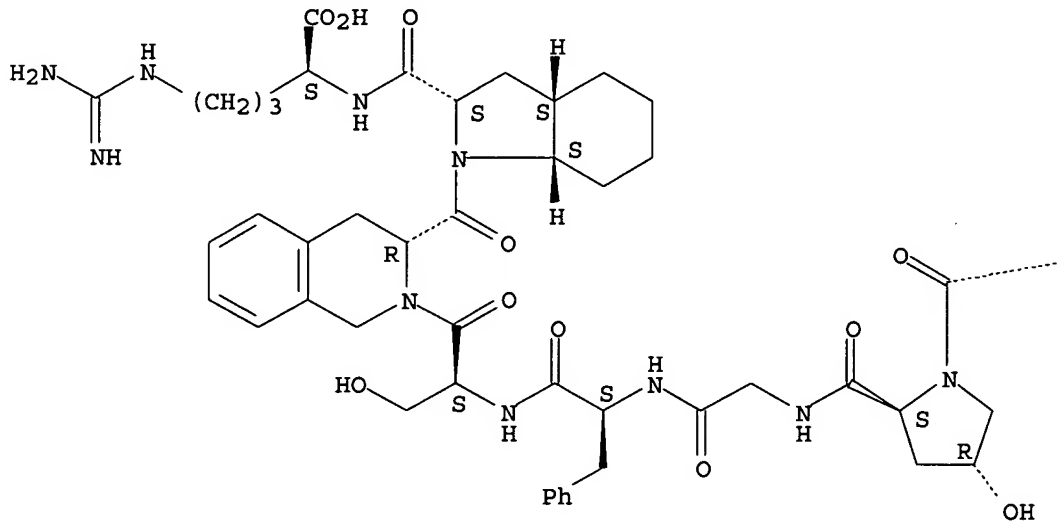


L29 ANSWER 12 OF 21 HCAPLUS COPYRIGHT 2005 ACS on STN
AN 1994:290682 HCAPLUS
DN 120:290682
ED Entered STN: 11 Jun 1994
TI A Proposed Model of Bradykinin Bound to the Rat B2 Receptor and Its Utility for Drug Design
AU Kyle, Donald J.; Chakravarty, Sarvajit; Sinsko, Jacqueline A.; Stormann, Thomas M.
CS Scios Nova Inc., Baltimore, MD, 21224, USA
SO Journal of Medicinal Chemistry (**1994**), 37(9), 1347-54
CODEN: JMCMAR; ISSN: 0022-2623
DT Journal
LA English
CC 2-10 (Mammalian Hormones)
Section cross-reference(s): 34
AB A putative model of bradykinin bound to the rat B2 receptor was generated using a combination of homol. modeling (from the known transmembrane structure of bacteriorhodopsin), energy minimization, mol. dynamics, and a two-stage conformational search as a docking simulation. Overall, the proposed bound ligand adopts a twisted "S" shape, wherein a C-terminal β-turn is buried in the receptor just below the extracellular boundary of the cell membrane and the N-terminus is interacting with neg. charged residues in extracellular loop 3 of the receptor (most notably Asp268 and Asp286). Mutagenesis expts. describing mutations which result in both a loss of bradykinin affinity as well as those which have no effect on bradykinin affinity are in good agreement with the proposed structure. In short, the mutagenesis results and the computational simulations each point to the same region of the receptor as likely to bind bradykinin. A double mutation, predicted as being likely to have a dramatic effect on bradykinin binding affinity, was confirmed exptl., adding some validation to the proposed complex. Moreover, a new pseudopeptide bradykinin receptor antagonist (D-Arg0-Arg1-[12-aminododecanoyl]2-Ser3-D-Tic4-Oic5-Arg6) was designed on the basis of the model, and found to have good receptor affinity. Speculation regarding other possible sites for mutagenesis are also described.

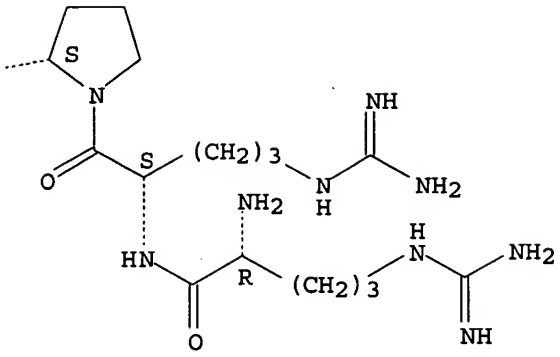
ST bradykinin receptor model antagonist; pseudopeptide bradykinin antagonist
IT Receptors
RL: BIOL (Biological study)
(bradykinin B2, bradykinin binding to, model for)
IT **130334-55-3P** 154939-24-9P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation and bradykinin antagonist activity of)
IT **130334-55-3P** 154939-24-9P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation and bradykinin antagonist activity of)
IT **130334-55-3P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation and bradykinin antagonist activity of)
RN 130334-55-3 HCAPLUS
CN Bradykinin, N2-D-arginyl-3-(trans-4-hydroxy-L-proline)-7-(D-1,2,3,4-tetrahydro-3-isoquinolinecarboxylic acid)-8-[L-(2α,3aβ,7aβ)-octahydro-1H-indole-2-carboxylic acid]- (9CI)
(CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



L29 ANSWER 13 OF 21 HCAPLUS COPYRIGHT 2005 ACS on STN
AN 1994:208607 HCAPLUS
DN 120:208607
ED Entered STN: 30 Apr 1994
TI Bradykinin antagonists for the treatment of acute pancreatitis
IN Griesbacher, Thomas; Lembeck, Fred
PA Hoechst A.-G., Germany
SO Eur. Pat. Appl., 16 pp.
CODEN: EPXXDW
DT Patent
LA English
IC ICM C07K007-18
ICS A61K037-02
CC 1-9 (Pharmacology)
FAN.CNT 1

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PI	EP 548825	A1	19930630	EP 1992-121558	19921218	<--
	EP 548825	B1	19970507			
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	AU 9230212	A1	19930624	AU 1992-30212	19921217	<--
	AU 662188	B2	19950824			
	CA 2085781	AA	19930622	CA 1992-2085781	19921218	<--
	CA 2085781	C	20030923			
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	JP 3588472	B2	20041110			
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	ES 2101017	T3	19970701	ES 1992-121558	19921218	<--
	CN 1073603	A	19930630	CN 1992-114564	19921221	<--
	HU 63336	A2	19930830	HU 1992-4074	19921221	<--
	HU 214056	B	19971229			
	US 5670619	A	19970923	US 1994-232338	19940422	<--

PRAI EP 1991-122055 A 19911221 <--
US 1992-992096 B1 19921217 <--

CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES	
EP 548825	ICM	C07K007-18	
	ICS	A61K037-02	
EP 548825	ECLA	A61K038/04E	<--
US 5670619	NCL	530/314.000; 530/328.000	
	ECLA	A61K038/08	<--

OS MARPAT 120:208607

AB Bradykinin antagonists R1-A-B-C-E-F-G-J-K-R2 (R1 = H, C1-4 alkanoyl, optionally substituted by mercapto, hydroxyphenyl, (4-benzoyl)phenoxy, (4-benzoyl)benzoyl-Lys; A = D-Arg, D-Lys, a direct bond; B = Arg optionally substituted by NO2 or toluol-4-sulfonyl, Lys optionally substituted by toluol-4-sulfonyl or CO-NH-C6H5, or a direct bond; C = Hyp-Pro-Gly, Pro-Hyp-Gly, Pro-Pro-Gly, dehydroPro-Hyp-Gly; E = Thi, Phe, Leu, Cha; F = Ser, Cys; G = D-Tic, D-Phe or D-Hyp substituted by C1-C4-alkoxy; J = Tic, Aoc, Oic; K = Arg, Ahx, direct bond; R2 is hydroxy or amino) and the physiol. tolerable salts thereof are used for the treatment of acute pancreatitis. The peptide H-D-Arg-Arg-Pro-Gly-Thi-Ser-D-Tic-Oic-Arg-OH was tested for its effects on exogenous bradykinin synthesis in rabbits and on exptl. pancreatitis in rats. The peptide at 3 nmol/kg completely inhibited the fall in blood pressure induced by kallikrein 10 nmol/kg or kallikrein 10 U/kg. Treatment of rats with the peptide inhibited the development of caerulein-induced pancreatic edema (Evans Blue assay) but did potentiate the release of pancreatic lipase and amylase into the serum, thereby allowing the enzyme to leave the tissue without hindrance and so lessen complications associated with it.

ST pancreatitis acute bradykinin antagonist peptide

IT Pancreas, disease
(acute pancreatitis, treatment of, bradykinin antagonist peptides for)

IT 130308-48-4 **130308-49-5 130334-55-3** 147267-10-5
147836-85-9 153986-61-9
RL: BIOL (Biological study)
(bradykinin antagonist, for treatment of acyte pancreatitis)

IT 130308-48-4 **130308-49-5 130334-55-3** 147267-10-5
147836-85-9 153986-61-9
RL: BIOL (Biological study)
(bradykinin antagonist, for treatment of acyte pancreatitis)

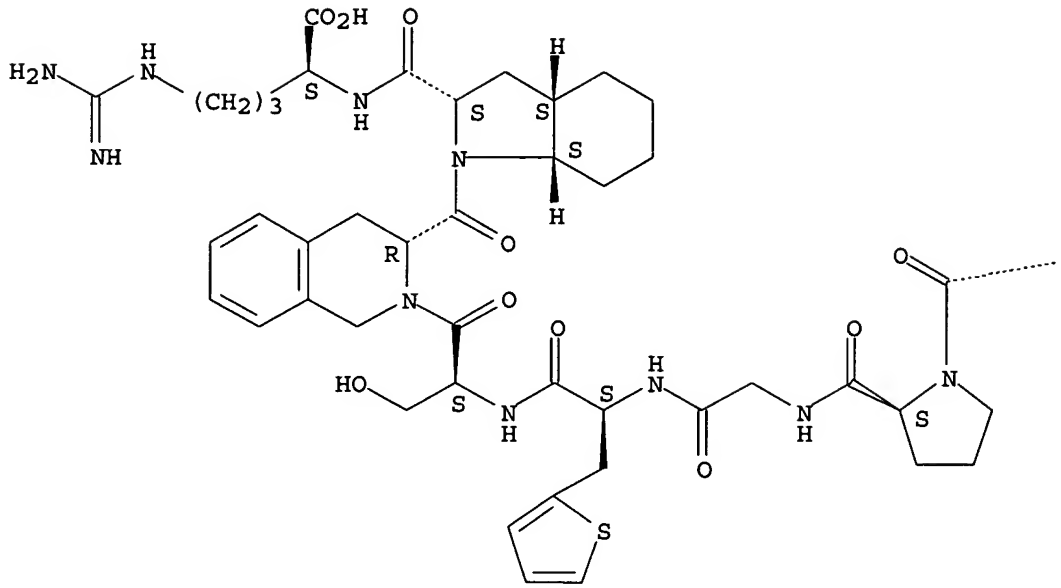
IT **130308-49-5 130334-55-3**
RL: BIOL (Biological study)
(bradykinin antagonist, for treatment of acyte pancreatitis)

RN 130308-49-5 HCAPLUS

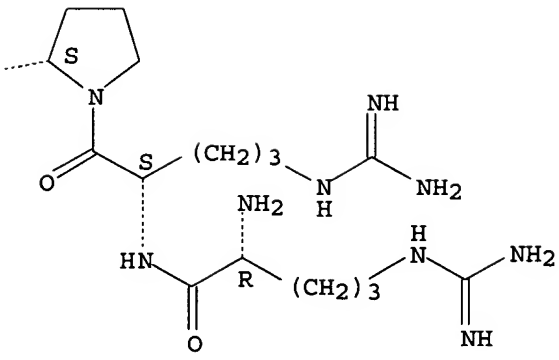
CN L-Arginine, D-arginyl-L-arginyl-L-prolyl-L-prolylglycyl-3-(2-thienyl)-L-alanyl-L-seryl-(3R)-1,2,3,4-tetrahydro-3-isoquinolinecarbonyl-(2S,3aS,7aS)-octahydro-1H-indole-2-carbonyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



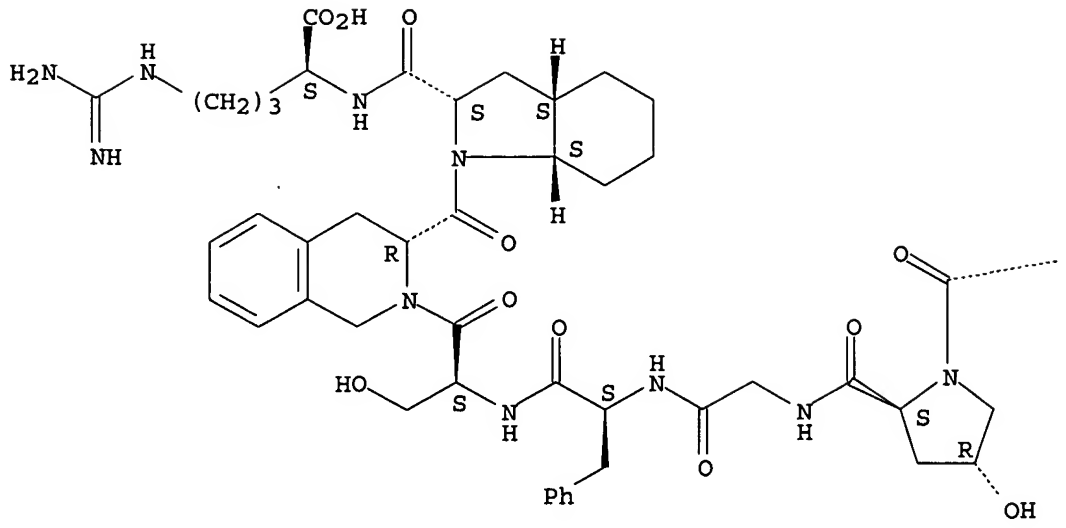
PAGE 1-B



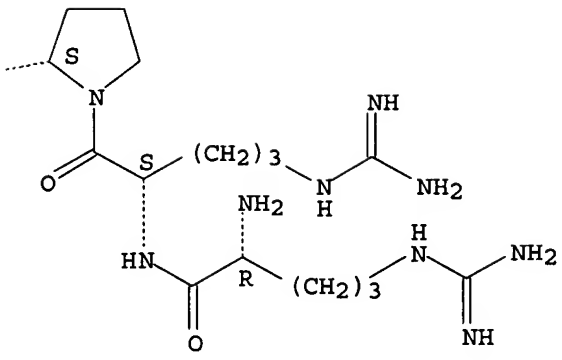
RN 130334-55-3 HCAPLUS
CN Bradykinin, N2-D-arginyl-3-(trans-4-hydroxy-L-proline)-7-(D-1,2,3,4-tetrahydro-3-isoquinolinecarboxylic acid)-8-[L-(2α,3aβ,7aβ)-octahydro-1H-indole-2-carboxylic acid]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



L29 ANSWER 14 OF 21 HCAPLUS COPYRIGHT 2005 ACS on STN
AN 1994:153920 HCAPLUS
DN 120:153920
ED Entered STN: 02 Apr 1994
TI Synthesis, Characterization, and Conformational Analysis of the D/L-Tic7 Stereoisomers of Bradykinin Receptor Antagonist D-Arg0[Hyp3,Thi5,D-Tic7,Oic8]bradykinin
AU Sawutz, David G.; Salvino, Joseph M.; Seoane, Peter R.; Douty, Brent D.; Houck, Wayne T.; Bobko, Mark A.; Doleman, Muriel S.; Dolle, Roland E.; Wolfe, Henry R.

CS Department of Enzymology and Receptor Biochemistry, Sterling Winthrop Pharmaceuticals Research Division, Collegeville, PA, 19426, USA
SO Biochemistry (**1994**), 33(9), 2373-9
CODEN: BICHAW; ISSN: 0006-2960
DT Journal
LA English
CC 2-2 (Mammalian Hormones)
Section cross-reference(s): 34
AB D-Arg0[Hyp3,Thi5,D-Tic7,Oic8]bradykinin (HOE-140) is a potent (Ki = 0.11 nM) inhibitor of [3H]bradykinin binding to bradykinin B2 receptors found on human IMR-90 fetal lung fibroblasts. During the synthesis of this compound, the authors isolated and unambiguously identified the L-Tic7 stereoisomer (WIN 65365), which exhibits a 2000-fold lower binding affinity (Ki = 130 nM) than HOE-140 to the bradykinin receptor. A similar decrease in potency is observed for WIN 65365 inhibition of bradykinin-stimulated 45Ca2+ efflux from IMR-90 cells. Both HOE-140 and WIN 65365 appear to be competitive antagonists at the IMR-90 bradykinin receptor. This is the first documentation of bradykinin binding and functional antagonist activity by a bradykinin peptide analog with an L amino acid replacing Pro7. To rationalize the differences in binding affinities of HOE-140 and WIN 65365, a conformational anal. of the peptides was undertaken using annealed mol. dynamics (AMD). Conformational anal. of HOE-140 reveals a strong preference for the formation of a type II' β-turn in the carboxy-terminal region. Analogous modeling of WIN 65365 reveals that its conformation is strikingly different from HOE-140 in that the four carboxy-terminal residues of WIN 65365 do not form a β-turn. These differences in low-energy conformations between the two peptides may lead to a better understanding of the mol. interaction of antagonists with the bradykinin receptor.
ST bradykinin receptor antagonist; conformation WIN 65365 HOE 140
IT Lung, composition
(bradykinin B2 receptors in, HOE-140 and WIN 65365 binding to, from human fetus)
IT Fibroblast
(of lung, HOE-140 and WIN 65365 binding to bradykinin B2 receptors in, from human fetus)
IT Receptors
RL: BIOL (Biological study)
(bradykinin B2, HOE-140 and WIN 65365 binding to, in human fetal lung fibroblasts, conformation in relation to)
IT Molecular structure-biological activity relationship
(bradykinin receptor-binding, of HOE-140 and WIN 65365, in human fetal lung fibroblasts)
IT Biological transport
(efflux, of calcium, HOE-140 and WIN 65365 inhibition of bradykinin stimulation of, from human fetal lung fibroblasts)
IT Embryo
(fetus, bradykinin B2 receptors in lung fibroblasts of, HOE-140 and WIN 65365 binding to, from human)
IT Conformation and Conformers
(β-turn, type II', of HOE-140 and WIN 65365, as bradykinin receptor antagonists)
IT 97825-00-8, [D-Phe7]bradykinin
RL: BIOL (Biological study)
(binding of, to bradykinin B2 receptors from human fetal lung fibroblasts, HOE-140 and WIN 65365 in relation to)
IT 130308-48-4, HOE-140
RL: PRP (Properties)
(conformation of, as bradykinin B2 receptor antagonist in human fetal

lung fibroblasts)

IT 7440-70-2, Calcium, biological studies
RL: BIOL (Biological study)
(efflux of, HOE-140 and WIN 65365 inhibition of bradykinin stimulation of, from human fetal lung fibroblasts)

IT **153322-84-0P**, Win 65365
RL: PRP (Properties); SPN (Synthetic preparation); PREP (Preparation)
(preparation and conformation of, as bradykinin B2 receptor antagonist in human fetal lung fibroblasts)

IT **153322-84-0P**, Win 65365
RL: PRP (Properties); SPN (Synthetic preparation); PREP (Preparation)
(preparation and conformation of, as bradykinin B2 receptor antagonist in human fetal lung fibroblasts)

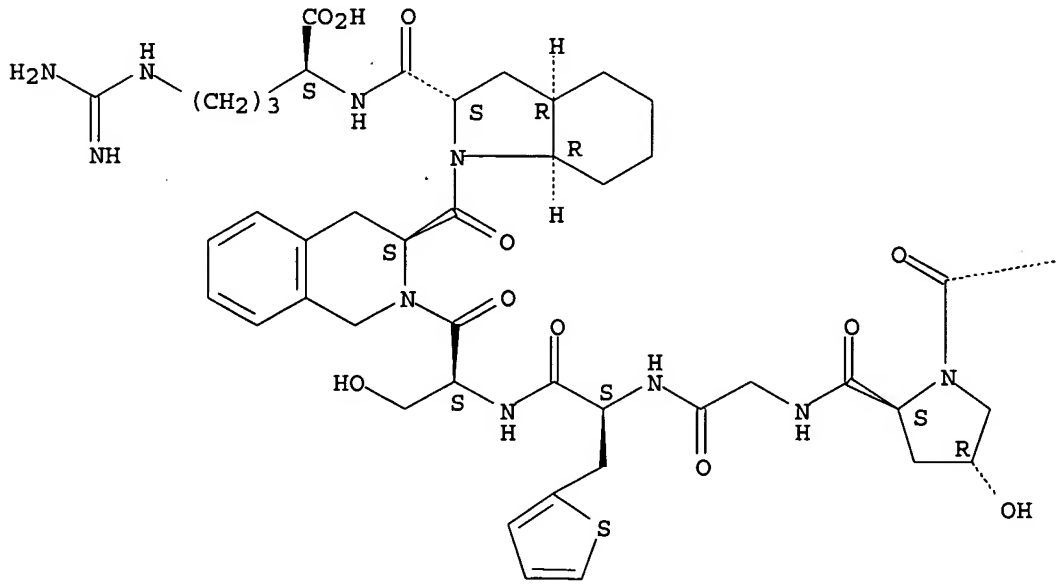
IT **153322-84-0P**, Win 65365
RL: PRP (Properties); SPN (Synthetic preparation); PREP (Preparation)
(preparation and conformation of, as bradykinin B2 receptor antagonist in human fetal lung fibroblasts)

RN 153322-84-0 HCAPLUS

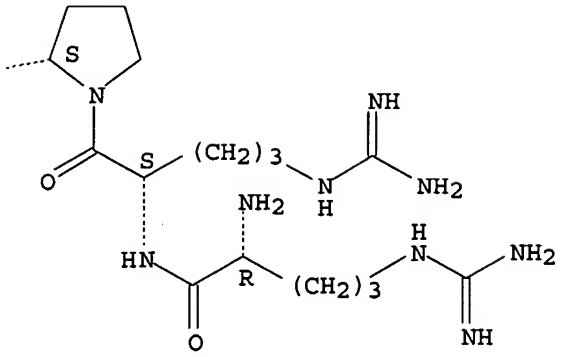
CN L-Arginine, D-arginyl-L-arginyl-L-prolyl-trans-4-hydroxy-L-prolylglycyl-3-(2-thienyl)-L-alanyl-L-seryl-L-1,2,3,4-tetrahydro-3-isoquinolinecarbonyl-L-(2α,3aβ,7aβ)-octahydro-1H-indole-2-carbonyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B

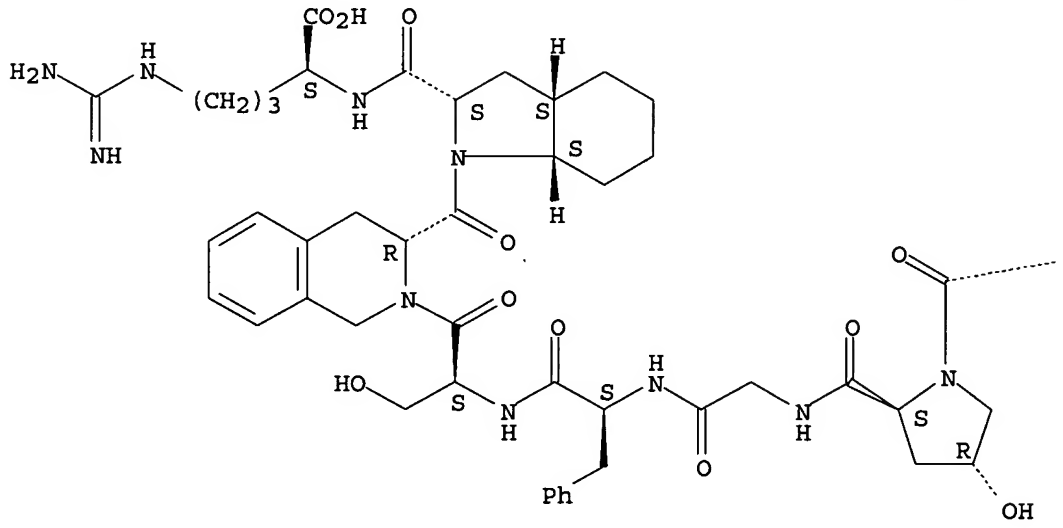


L29 ANSWER 15 OF 21 HCAPLUS COPYRIGHT 2005 ACS on STN
AN 1993:650452 HCAPLUS
DN 119:250452
ED Entered STN: 11 Dec 1993
TI Design of potent, cyclic peptide bradykinin receptor antagonists from conformationally constrained linear peptides
AU Chakravarty, Sarvajit; Wilkins, Deidre; Kyle, Donald J.
CS Scios Nova Inc., Baltimore, MD, 21224, USA
SO Journal of Medicinal Chemistry (**1993**), 36(17), 2569-71
CODEN: JMCMAR; ISSN: 0022-2623
DT Journal
LA English
CC 34-3 (Amino Acids, Peptides, and Proteins)
Section cross-reference(s): 1
AB Beginning with a prototypical second generation peptide bradykinin receptor antagonist, D-Arg0-Arg1-Pro2-Hyp3-Gly4-Phe5-Ser6-D-Tic7-Oic8-Arg9 (I), a series of backbone-constrained analogs were prepared Specifically, N- and/or Cα-Me substitution was made either to Gly4, Phe5, or both. With the exception of D-Arg0-Arg1-Pro2-Hyp3-Gly4-[Cα-methyl]Phe5-Ser6-D-Tic7-Oic8-Arg9 (II), all of these constrained peptides lost affinity for the receptor by at least 1000-fold with respect to I. II however, had a Ki of 0.52 nM, which was only slightly less than that of I. This led to the conclusion that the ϕ,ψ backbone dihedral angles about Phe5 were likely close to -60°, -60° or kinked into a twist in the biol.-active from. To test this hypothesis, two cyclic peptides were prepared, D-Arg0-Arg1-Cys2-Pro3-Gly4-Cys5-Ser6-D-Tic7-Oic8-Arg9 and D-Arg0-Arg1-Cys2-Pro3-Gly4-Phe5-Cys6-D-Tic7-Oic8-Arg9. Each of these peptides were cyclized through their inherent two Cys side chain groups and had Kis against the B2 bradykinin receptor of 1.5 nM, and 14.8 nM, resp. These first examples of potent cyclic bradykinin receptor antagonists may ultimately provide insight into the biol.-active conformation(s) of related peptide antagonists via spectroscopic expts.
ST bradykinin antagonist cyclic peptide
IT Receptors
RL: RCT (Reactant); RACT (Reactant or reagent)

(bradykinin, antagonists, cyclic peptides)
IT Peptides, preparation
RL: SPN (Synthetic preparation); PREP (Preparation)
(cyclo-, preparation as bradykinin antagonists)
IT **130334-55-3**
RL: RCT (Reactant); RACT (Reactant or reagent)
(analogs, preparation as bradykinin antagonists)
IT 58-82-2, Bradykinin
RL: RCT (Reactant); RACT (Reactant or reagent)
(antagonists, cyclic peptides)
IT 150629-59-7 150629-60-0 150629-61-1 150629-62-2 150629-63-3
150629-64-4 150629-65-5 150629-66-6
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation as bradykinin antagonist)
IT **130334-55-3**
RL: RCT (Reactant); RACT (Reactant or reagent)
(analogs, preparation as bradykinin antagonists)
RN 130334-55-3 HCAPLUS
CN Bradykinin, N2-D-arginyl-3-(trans-4-hydroxy-L-proline)-7-(D-1,2,3,4-tetrahydro-3-isoquinolinecarboxylic acid)-8-[L-(2α,3aβ,7aβ)-octahydro-1H-indole-2-carboxylic acid]- (9CI)
(CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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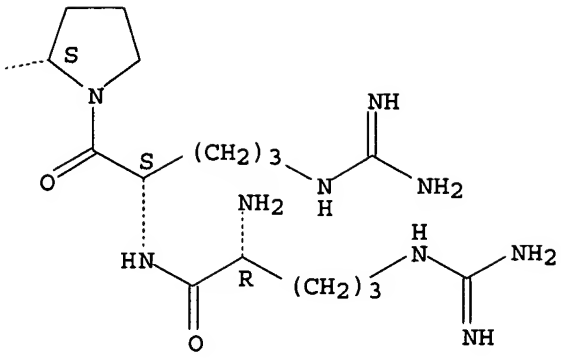
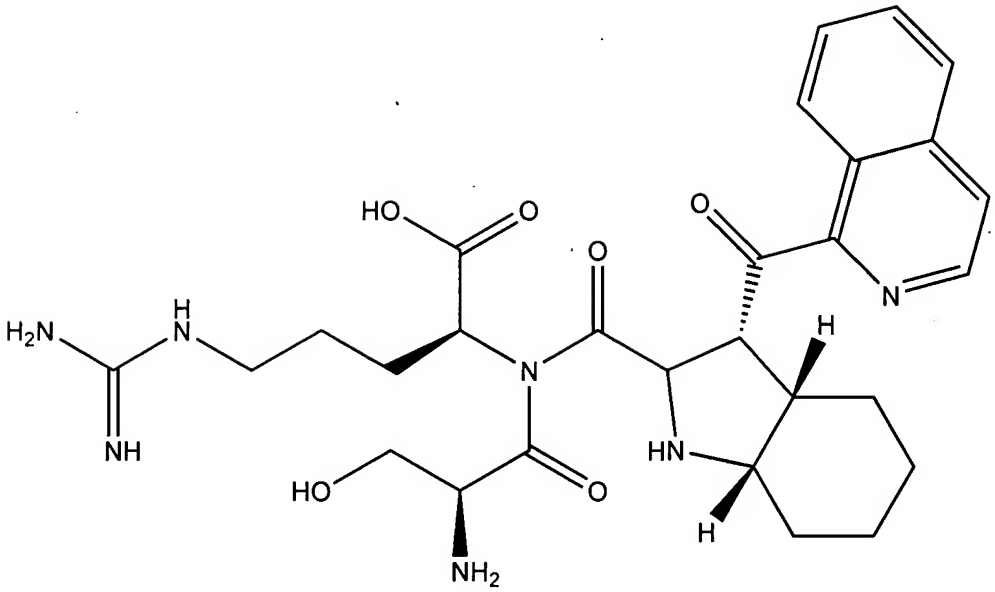


L29 ANSWER 16 OF 21 HCAPLUS COPYRIGHT 2005 ACS on STN
AN 1993:620793 HCAPLUS
DN 119:220793
ED Entered STN: 27 Nov 1993
TI Chirality determinations of D- and L-amino acids of synthetic and naturally occurring peptides
AU Purcell, Brenda L.; Doleman, Muriel S.
CS Pharm. Res. Div., Sterling Winthrop, Great Valley, PA, 19355, USA
SO Tech. Protein Chem. IV, [Pap. Protein Soc. Symp.], 6th (**1993**), Meeting Date 1992, 315-21. Editor(s): Angeletti, Ruth Hogue. Publisher: Academic, San Diego, Calif.
CODEN: 59INA3
DT Conference
LA English
CC 9-3 (Biochemical Methods)
Section cross-reference(s): 2, 34
AB Reversed phase HPLC was used for separating hydrolyzed peptide derivatized with the chiral reagent 1-fluoro-2,4-dinitrophenyl-5-L-alanine amide (Marfey's reagent). Synthetic peptide Woc-114-108 was used as an example.
ST peptide amino acid HPLC; Marfey reagent peptide HPLC; liq chromatog peptide Marfey reagent
IT Amino acids, analysis
Peptides, analysis
RL: ANST (Analytical study)
(separation of, by reversed-phase-HPLC, chirality determination with Marfey reagent)
IT Chromatography, column and liquid
(high-performance reversed-phase, for amino acid and peptide separation, chirality determination with Marfey's reagent in)
IT 95713-52-3, Marfey's reagent
RL: ANST (Analytical study)
(in amino acid chirality determination of hydrolyzed peptides)
IT 95713-52-3, Marfey's reagent
RL: ANST (Analytical study)
(in amino acid chirality determination of hydrolyzed peptides)

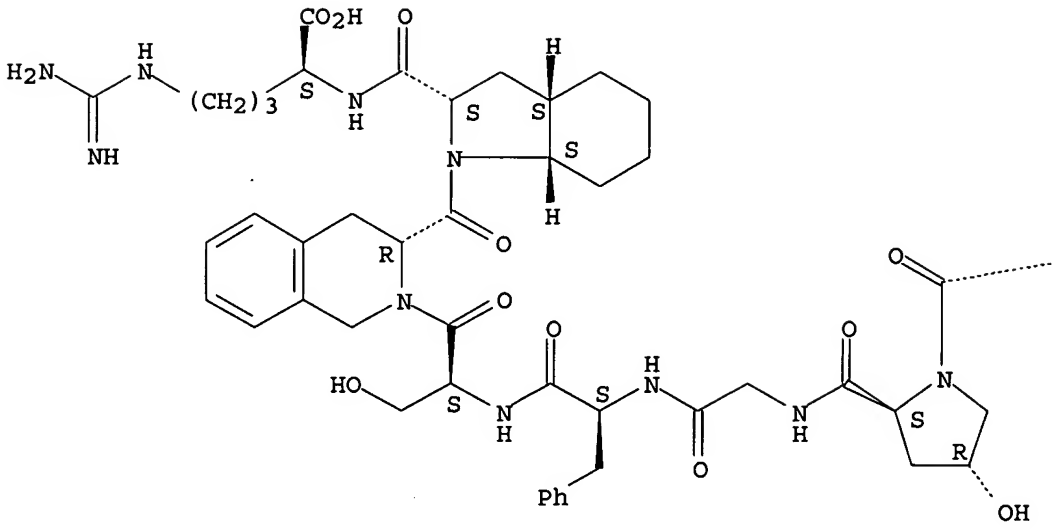


l-seryl-(3R)-1,2,3,4-tetrahydro-3-isoquinolinecarbonyl-(2S-3aS-7aS)-octahydro-1H-indole-2-carbonyl-L-arginine

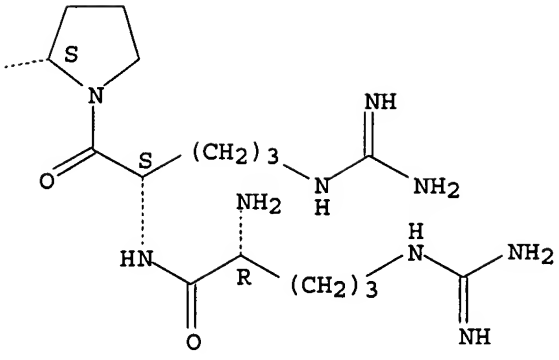
L29 ANSWER 17 OF 21 HCAPLUS COPYRIGHT 2005 ACS on STN
AN 1993:441697 HCAPLUS
DN 119:41697
ED Entered STN: 07 Aug 1993
TI Lack of significant unspecific effects of HOE 140 and other novel bradykinin antagonists in vitro and in vivo
AU Lembeck, F.; Griesbacher, T.; Legat, F. J.
CS Dep. Exp. Clin. Pharmacol., Univ. Graz, Graz, A-8010, Australia
SO Agents and Actions Supplements (**1992**), (2, Recent Prog. Kinins: Pharmacol. Clin. Aspects Kallikrein-Kinin Syst., Pt. 1), 414-22
CODEN: AASUDJ; ISSN: 0379-0363
DT Journal
LA English
CC 2-10 (Mammalian Hormones)
Section cross-reference(s): 1
AB The novel, potent and long-acting bradykinin (BK) antagonists, HOE 140 and related compds., slightly decreased blood pressure, but did not affect heart rate and respiration of rats. The antagonists did not cause bronchoconstriction in guinea pigs. Neither HOE 140 nor BK released histamine from isolated perfused hindlegs of rats. The lack of significant unspecific side effects of the novel antagonists of EDs will further increase the usefulness of these compds. for exptl. and therapeutic purposes.
ST HOE 140 bradykinin antagonist
IT 130308-48-4, HOE 140 **130334-55-3** 140695-51-8.
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(as bradykinin antagonist, side effects of)
IT **130334-55-3**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(as bradykinin antagonist, side effects of)
RN 130334-55-3 HCAPLUS
CN Bradykinin, N2-D-arginyl-3-(trans-4-hydroxy-L-proline)-7-(D-1,2,3,4-tetrahydro-3-isoquinolinecarboxylic acid)-8-[L-(2α,3aβ,7aβ)-octahydro-1H-indole-2-carboxylic acid]- (9CI)
(CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



L29 ANSWER 18 OF 21 HCAPLUS COPYRIGHT 2005 ACS on STN
AN 1993:261015 HCAPLUS
DN 118:261015
ED Entered STN: 26 Jun 1993
TI Compositions for topical administration to the nose or the eyes containing bradykinin antagonists
IN Seidel, Heinz Ruediger; Wirth, Klaus; Giessler, Norbert
PA Hoechst A.-G., Germany
SO Eur. Pat. Appl., 8 pp.
CODEN: EPXXDW

DT Patent
LA German
IC ICM C07K007-18
ICS A61K009-08
CC 63-6 (Pharmaceuticals)
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI EP 529499	A1	19930303	EP 1992-114145	19920819 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
HU 63060	A2	19930728	HU 1992-2690	19920819 <--
CA 2076558	AA	19930223	CA 1992-2076558	19920821 <--
NO 9203293	A	19930223	NO 1992-3293	19920821 <--
AU 9221245	A1	19930225	AU 1992-21245	19920821 <--
ZA 9206313	A	19930428	ZA 1992-6313	19920821 <--
JP 05221873	A2	19930831	JP 1992-222337	19920821 <--
PRAI DE 1991-4127738	A	19910822 <--		

CLASS

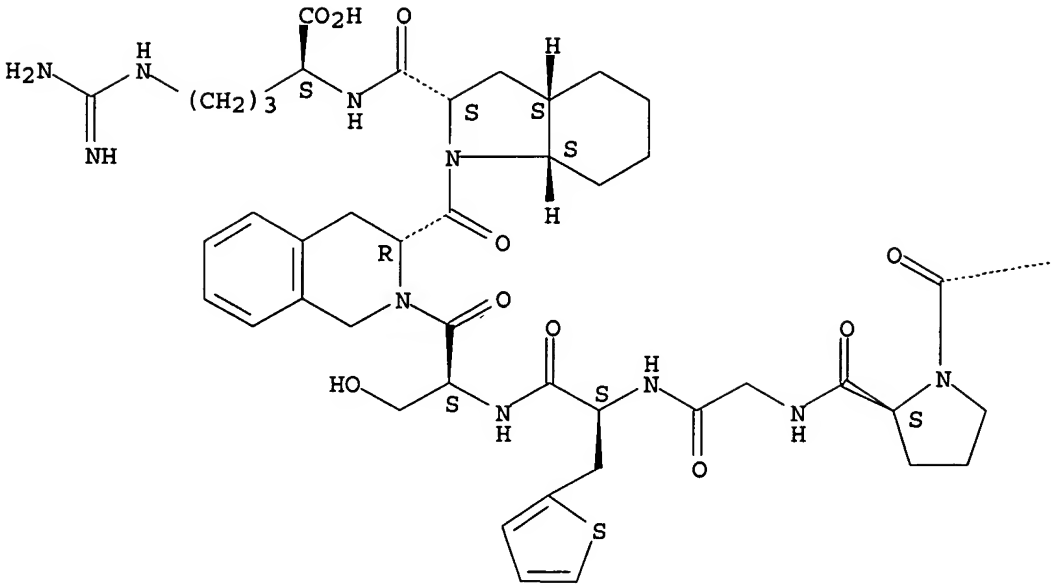
PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
EP 529499	ICM	C07K007-18
	ICS	A61K009-08

AB Bradykinin antagonists are formulated as drops, sprays, gels, and ointments for nasal and ophthalmic application. The compns., which are buffered and isotonized, comprise a solvent, a preservative, and optionally, a thickening agent or ointment base. A nasal spray comprised HOE-140 50.0, HAcO 6.2, NaAcO.3H2O 165.5, benzalkonium chloride 10.0, NaCl 835.0 mg, and H2O to 100 g.

ST bradykinin antagonist nasal ophthalmic prepn
IT Pharmaceutical dosage forms
(ophthalmic, bradykinin antagonists-containing)
IT Pharmaceutical dosage forms
(sprays, nasal, bradykinin antagonists-containing)
IT 58-82-2, Bradykinin
RL: BIOL (Biological study)
(antagonists, formulation of, as nasal and ophthalmic preparation)
IT 130308-48-4 **130308-49-5 130334-55-3** 140695-51-8
147820-70-0 147836-85-9 147921-72-0
RL: BIOL (Biological study)
(bradykinin antagonist, formulation of, as nasal and ophthalmic preparation)
IT **130308-49-5 130334-55-3**
RL: BIOL (Biological study)
(bradykinin antagonist, formulation of, as nasal and ophthalmic preparation)
RN 130308-49-5 HCAPLUS
CN L-Arginine, D-arginyl-L-arginyl-L-prolyl-L-prolylglycyl-3-(2-thienyl)-L-alanyl-L-seryl-(3R)-1,2,3,4-tetrahydro-3-isoquinolinecarbonyl-(2S,3aS,7aS)-octahydro-1H-indole-2-carbonyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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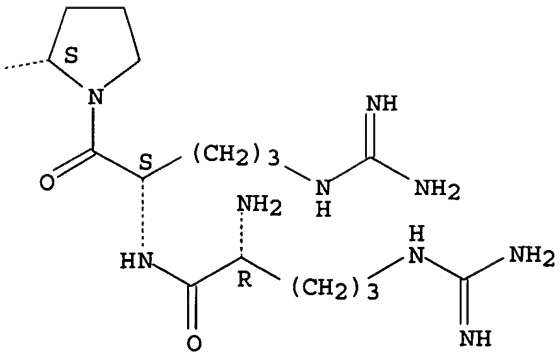
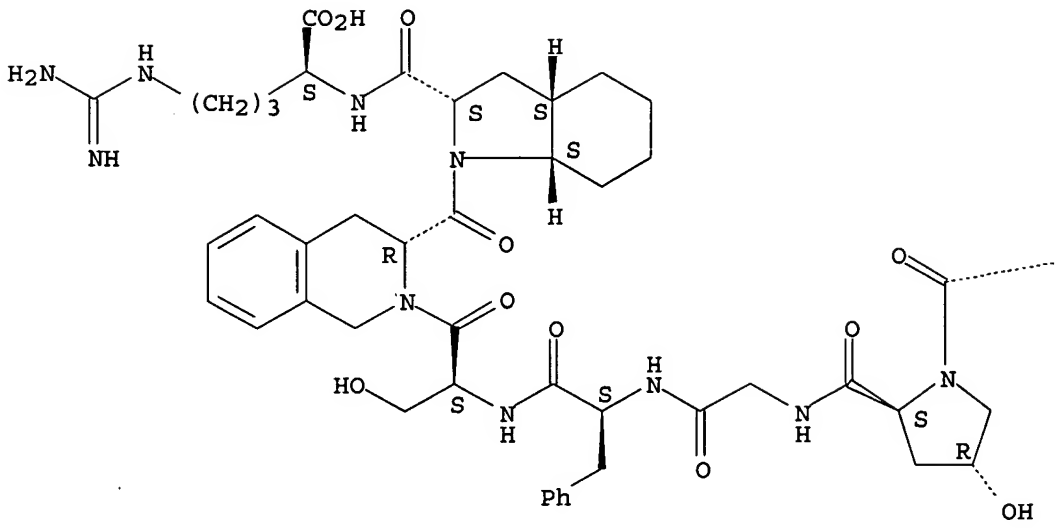


RN 130334-55-3 HCAPLUS
CN Bradykinin, N2-D-arginyl-3-(trans-4-hydroxy-L-proline)-7-(D-1,2,3,4-tetrahydro-3-isoquinolinecarboxylic acid)-8-[L-(2α,3aβ,7aβ)-octahydro-1H-indole-2-carboxylic acid]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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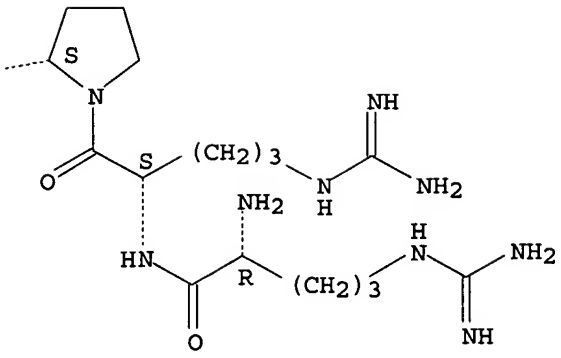
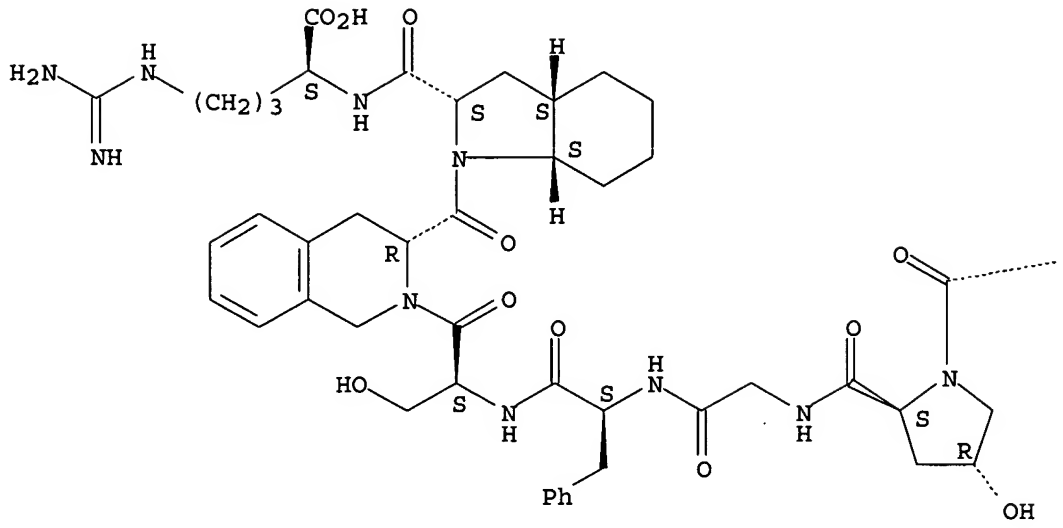


L29 ANSWER 19 OF 21 HCAPLUS COPYRIGHT 2005 ACS on STN
AN 1992:188596 HCAPLUS
DN 116:188596
ED Entered STN: 16 May 1992
TI Analysis of the antagonistic actions of HOE 140 and other novel bradykinin analogues on the guinea pig ileum
AU Griesbacher, Thomas; Lembeck, Fred
CS Clin. Pharmacol., Univ. Graz, Graz, A-8010, Austria
SO European Journal of Pharmacology (**1992**), 211(3), 393-8
CODEN: EJPHAZ; ISSN: 0014-2999

DT Journal
LA English
CC 2-10 (Mammalian Hormones)
AB The type of antagonism exhibited by three novel bradykinin (BK) antagonists, D-Arg-[Hyp3,Thi5,D-Tic7,Oic8]BK (HOE 140, I) D-Arg-{Hyp3,D-Tic7,Oic8]BK (II) and [Arg(Tos)1,Hyp3,Thi5,D-Tic7,Oic8]BK (III), was compared with that of a conventional antagonist, D-Arg-[Hyp2,Thi5,8,D-Phe7]BK (IV), on the guinea pig ileum. The novel compds. induced rightward displacements of cumulative concentration-response curves to BK, accompanied by a progressive reduction of the maximum effect (Emax) without a significant decrease in the slope, whereas no reduction of Emax was observed with IV. Actions of substance P on the guinea pig ileum and of vasopressin on the rat uterus remained completely unaffected. It is concluded that as the novel BK analogs show competitive as well as non-competitive inhibition in the guinea pig ileum, but the inhibition is reversible and specific, they are dual antagonists.
ST bradykinin receptor antagonist ileum muscle HOE140
IT Receptors
RL: BIOL (Biological study)
(bradykinin, HOE 140 and other bradykinin analogs antagonism of, in ileum)
IT Intestine, composition
(ileum, bradykinin receptors of smooth muscle of, HOE 140 and other bradykinin analogs antagonism of)
IT 58-82-2D, Bradykinin, analogs 103412-42-6 130308-48-4, HOE 140 **130334-55-3** 140695-51-8
RL: BIOL (Biological study)
(bradykinin antagonism with, in ileum, mechanism of)
IT **130334-55-3**
RL: BIOL (Biological study)
(bradykinin antagonism with, in ileum, mechanism of)
RN 130334-55-3 HCAPLUS
CN Bradykinin, N2-D-arginyl-3-(trans-4-hydroxy-L-proline)-7-(D-1,2,3,4-tetrahydro-3-isoquinolinecarboxylic acid)-8-[L-(2α,3aβ,7aβ)-octahydro-1H-indole-2-carboxylic acid]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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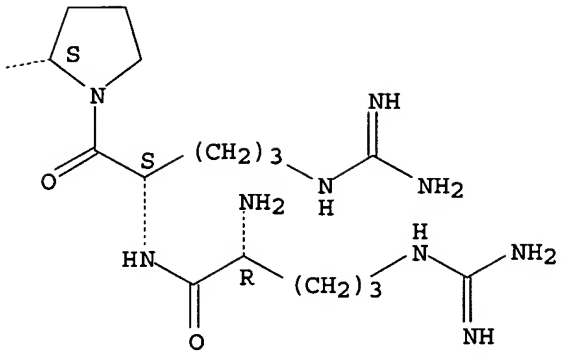

L29 ANSWER 20 OF 21 HCAPLUS COPYRIGHT 2005 ACS on STN
AN 1991:207831 HCAPLUS
DN 114:207831
ED Entered STN: 31 May 1991
TI Preparation of H-D-Argpeptidylarginines and analogs as bradykinin antagonists
IN Henke, Stephan; Anagnostopulos, Hinisto; Breipohl, Gerhard; Knolle, Jochen; Fehlhaber, Hans Wolfram; Stechl, Jens; Schoelkens, Berward
PA Hoechst A.-G., Germany
SO Ger. Offen., 26 pp.

CODEN: GWXXBX
DT Patent
LA German
IC ICM C07K007-18
ICS C07K007-06; A61K037-42
ICA C07K001-04; C07K001-06; C07K001-08; C07K001-10
CC 34-3 (Amino Acids, Peptides, and Proteins)
Section cross-reference(s): 1
FAN.CNT 4

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
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	FI 94353	B	19950515			
	FI 94353	C	19950825			
	NO 8903193	A	19900525	NO 1989-3193	19890808	<--
	NO 177597	B	19950710			
	NO 177597	C	19951018			
	AU 8939431	A1	19900531	AU 1989-39431	19890809	<--
	AU 612054	B2	19910627			
	ZA 8906068	A	19910130	ZA 1989-6068	19890809	<--
	CA 1340667	A1	19990720	CA 1989-607853	19890809	<--
	IL 91298	A1	19940530	IL 1989-91298	19890811	<--
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	SK 279315	B6	19980909	SK 1989-4906	19890821	<--
	HU 52527	A2	19900728	HU 1989-4323	19890823	<--
	HU 210566	B	19950529			
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	CN 1042918	A	19900613	CN 1989-107065	19890911	<--
	CN 1035006	B	19970528			
	KR 139632	B1	19980701	KR 1989-13102	19890911	<--
	EP 370453	A2	19900530	EP 1989-121498	19891121	<--
	EP 370453	A3	19911204			
	EP 370453	B1	19940615			
	R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE					
	ES 2057071	T3	19941016	ES 1989-121498	19891121	<--
	RU 2083586	C1	19970710	RU 1992-5052703	19921012	<--
	LV 10720	B	19960220	LV 1992-701	19921223	<--
	LT 3375	B	19950825	LT 1993-717	19930625	<--
PRAI	DE 1988-3839581	A1	19881124	<--		
	DE 1989-3916291	A1	19890519	<--		
	DE 1989-3918225	A1	19890603	<--		

CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES	
DE 3938751	ICM	C07K007-18	
	ICS	C07K007-06; A61K037-42	
	ICA	C07K001-04; C07K001-06; C07K001-08; C07K001-10	
EP 370453	ECLA	C07K007/18	<--

OS MARPAT 114:207831
GI For diagram(s), see printed CA Issue.
AB ABCEFK-(D)-TicGMF'-I [I; A = H, (un)substituted C1-8 alkyl, alkanoyl, alkoxycarbonyl, alkylsulfonyl, (un)substituted C3-8 cycloalkyl, carbamoyl, C6-12 aryl, C7-13 aryloyl, C3-9 heteroaryl, etc.; B = (un)substituted basic L- or D-amino acid residue; C = G'-G'-Gly, GNH(CH2)nCO; G' = NR4CHR5CO; R4R5 with the adjacent C and N atoms can form a heterocyclic

ring system; n = 2-8; E = aromatic amino acid residue; F = bond, amino acid residue; K = bond, NH(CH2)xCO; x = 1-4; D-Tic = Q; G = G', bond; M = F; F' = F, NH(CH2)n, bond when G ≠ bond; I = OH, NH2, NHEt] and their physiol. compatible salts, useful for the treatment of bradykinin-mediated pathol. states, e.g., wound, shock, burn, erythema, angina, arthritis, asthma, inflammations, hypotension, etc., were prepared by solid-phase peptide coupling. Approx. 160 I were prepared In an in vitro assay .apprx.25 I inhibited bradykinin-induced contraction of guinea pig pulmonal artery tissue with IC50 ranging from 2.6 + 10-5-4.2 + 10-9M.

ST arginylpeptidylarginine prepn bradykinin antagonist; peptide prepn bradykinin antagonist; shock treatment arginylpeptidylarginine prepn; burning treatment arginylpeptidylarginine prepn; burning treatment arginylpeptidylarginine prepn; erythema treatment arginylpeptidylarginine prepn; angina treatment arginylpeptidylarginine prepn; arthritis treatment arginylpeptidylarginine prepn; asthma treatment arginylpeptidylarginine prepn

IT Peptides, preparation
RL: SPN (Synthetic preparation); PREP (Preparation)
(arginylpeptidylarginines, preparation of, as bradykinin antagonists)

IT Molecular structure-biological activity relationship
(bradykinin receptor-binding, of arginylpeptidylarginines)

IT 35737-10-1 71989-20-3 78603-12-0 88050-17-3 98930-01-9D, benzyloxybenzyl alc. resin-bound 108321-39-7 109434-27-7 114119-85-6 114119-87-8 114119-90-3 119831-72-0 130309-33-0 130309-34-1 130309-35-2 130309-36-3 130309-37-4
RL: RCT (Reactant); RACT (Reactant or reagent)
(peptide coupling of, in preparation of bradykinin antagonist)

IT 130308-03-1P 130308-04-2P 130308-05-3P 130308-06-4P 130308-07-5P
130308-08-6P 130308-09-7P 130308-10-0P 130308-11-1P 130308-12-2P
130308-13-3P 130308-14-4P 130308-15-5P 130308-16-6P 130308-17-7P
130308-18-8P 130308-19-9P 130308-20-2P 130308-21-3P 130308-22-4P
130308-23-5P 130308-24-6P 130308-25-7P 130308-26-8P 130308-27-9P
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RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation of, as bradykinin antagonist)

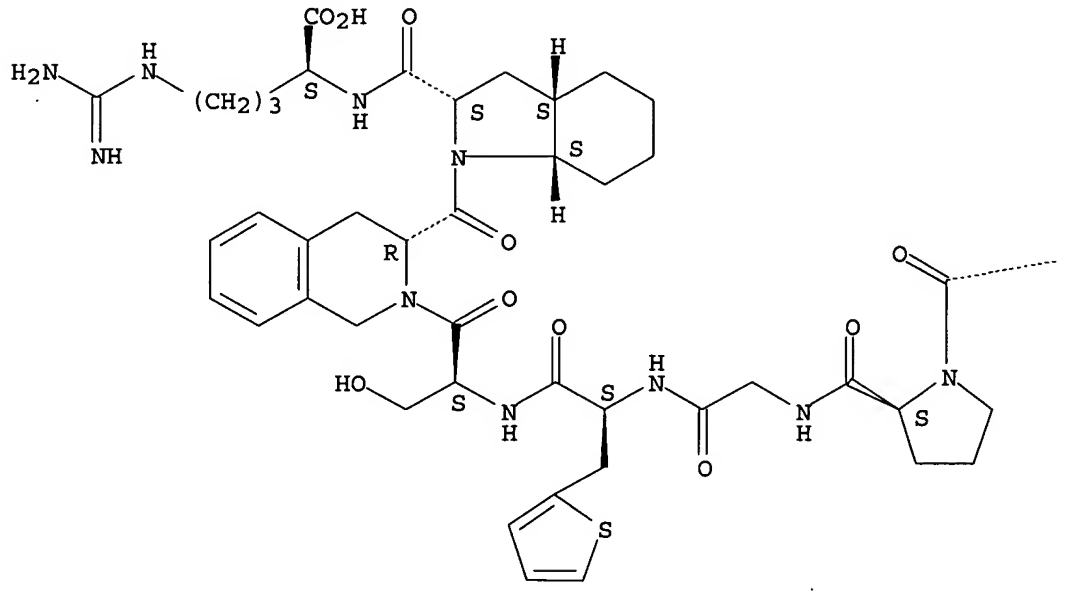
IT **130308-49-5P 130308-52-0P 130308-53-1P**
130334-55-3P 130404-96-5P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation of, as bradykinin antagonist)

RN 130308-49-5 HCAPLUS

CN L-Arginine, D-arginyl-L-arginyl-L-prolyl-L-prolylglycyl-3-(2-thienyl)-L-alanyl-L-seryl-(3R)-1,2,3,4-tetrahydro-3-isoquinolinecarbonyl-(2S,3aS,7aS)-octahydro-1H-indole-2-carbonyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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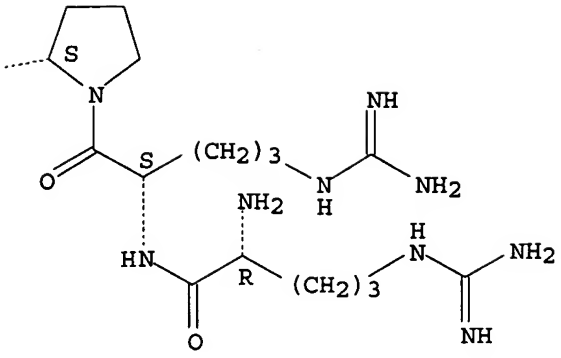
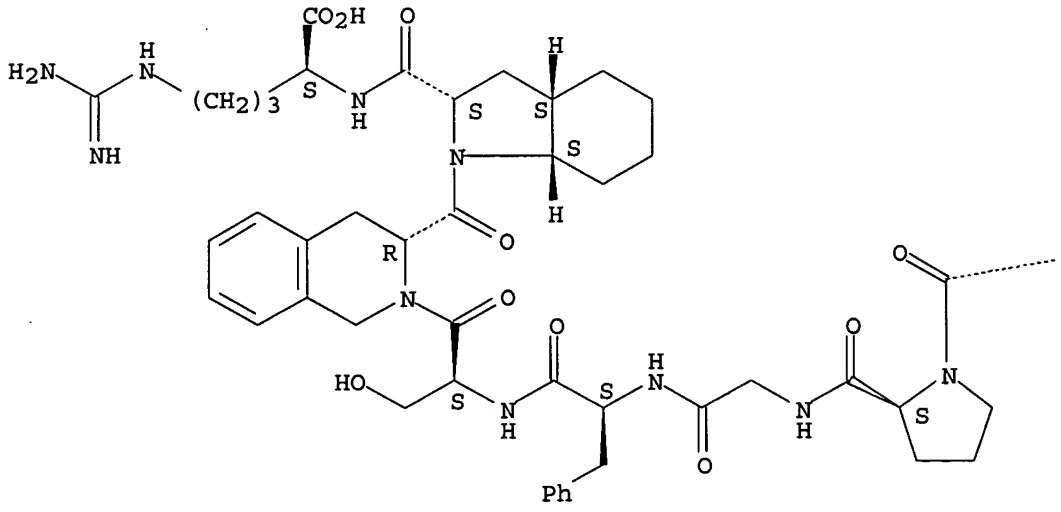


RN 130308-52-0 HCAPLUS
CN Bradykinin, N2-D-arginyl-2-(trans-4-hydroxy-L-proline)-7-(D-1,2,3,4-tetrahydro-3-isoquinolinecarboxylic acid)-8-[(2α,3aβ,7aβ)-L-octahydro-1H-indole-2-carboxylic acid]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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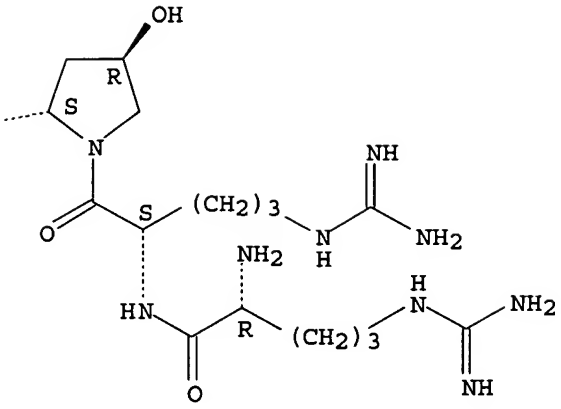
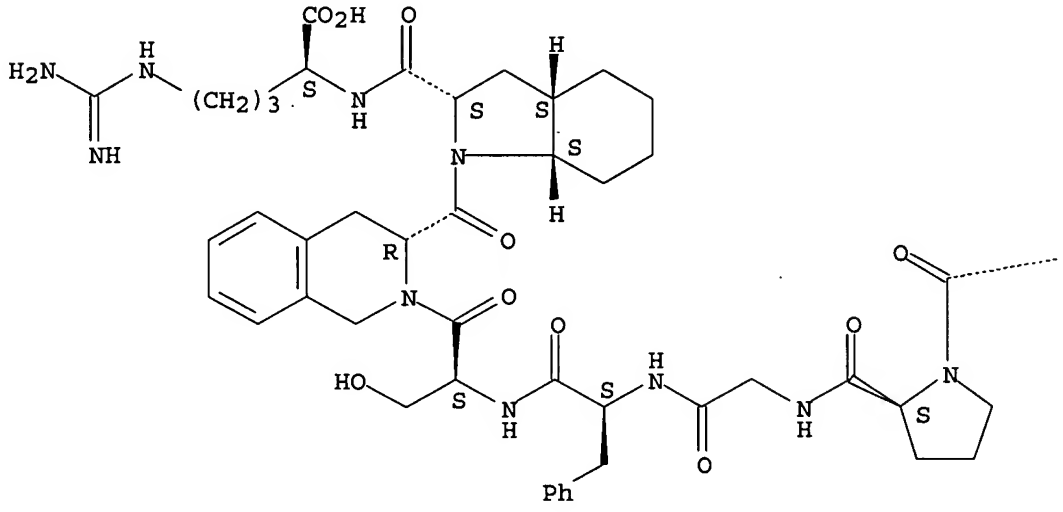


RN 130308-53-1 HCAPLUS
CN Bradykinin, N2-D-arginyl-7-(D-1,2,3,4-tetrahydro-3-isoquinolinecarboxylic acid)-8-[(2α,3aβ,7aβ)-L-octahydro-1H-indole-2-carboxylic acid]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



http://www.cas.org/ONLINE/DBSS/registryss.html

=> => s l14 not l25
L31 1 L14 NOT L25

=> d sqide can

L31 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2005 ACS on STN
RN 130308-48-4 REGISTRY
CN L-Arginine, D-arginyl-L-arginyl-L-prolyl-(4R)-4-hydroxy-L-prolylglycyl-3-(2-thienyl)-L-alanyl-L-seryl-(3R)-1,2,3,4-tetrahydro-3-isoquinolinecarbonyl-(2S,3aS,7aS)-octahydro-1H-indole-2-carbonyl- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN L-Arginine, D-arginyl-L-arginyl-L-prolyl-trans-4-hydroxy-L-prolylglycyl-3-(2-thienyl)-L-alanyl-L-seryl-D-1,2,3,4-tetrahydro-3-isoquinolinecarbonyl-L-(2α,3aβ,7aβ)-octahydro-1H-indole-2-carbonyl-
OTHER NAMES:
CN Icatibant
FS PROTEIN SEQUENCE; STEREOSEARCH
SQL **10**
NTE

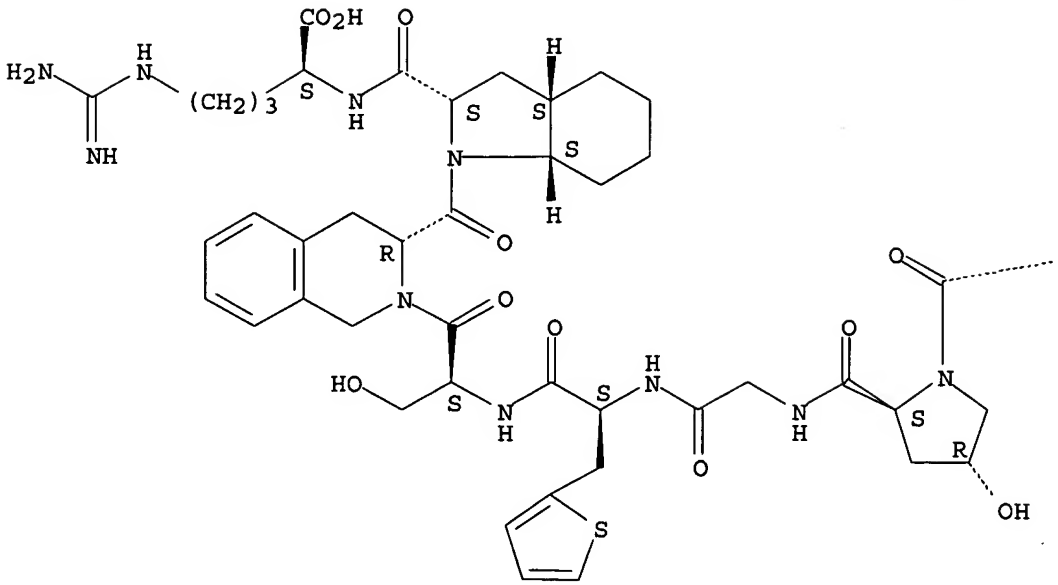
type	------ location ------		description
uncommon	Hyp-4	-	-
uncommon	Thi-6	-	-
uncommon	Tic-8	-	-
uncommon	Oic-9	-	-

SEQ 1 RRPXGXSXXR

RELATED SEQUENCES AVAILABLE WITH SEQLINK
DR 133404-66-7
MF **C59 H89 N19 O13 S**
CI COM
SR CA
LC STN Files: ADISINSIGHT, ADISNEWS, AGRICOLA, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CANCERLIT, CAPLUS, CASREACT, CHEMCATS, CIN, DDFU, DRUGU, EMBASE, IMSDRUGNEWS, IMSPATENTS, IMSRESEARCH, IPA, MEDLINE, PHAR, PROMT, PROUSDDR, RTECS*, TOXCENTER, USAN, USPAT2, USPATFULL
(*File contains numerically searchable property data)
DT.CA CAplus document type: Conference; Journal; Patent
RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); PRP (Properties); USES (Uses)
RLD.P Roles for non-specific derivatives from patents: BIOL (Biological study); USES (Uses)
RL.NP Roles from non-patents: ANST (Analytical study); BIOL (Biological study); MSC (Miscellaneous); PREP (Preparation); PROC (Process); PRP (Properties); RACT (Reactant or reagent); USES (Uses)
RLD.NP Roles for non-specific derivatives from non-patents: BIOL (Biological study)

Absolute stereochemistry.

PAGE 1-A



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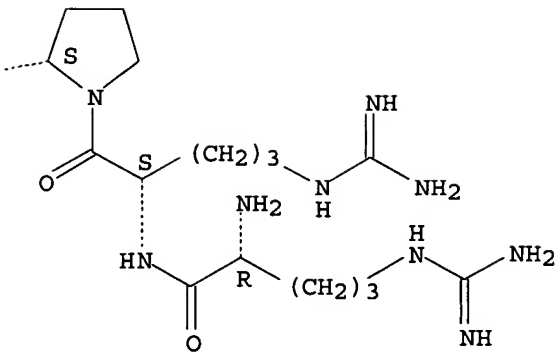

119 REFERENCES IN FILE CA (1907 TO DATE)
2 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
119 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 143:125696

REFERENCE 2: 143:90000

REFERENCE 3: 142:107809

REFERENCE 4: 141:388394

REFERENCE 5: 141:325451

REFERENCE 6: 141:307254

REFERENCE 7: 141:33934

REFERENCE 8: 140:423566

REFERENCE 9: 140:53082

REFERENCE 10: 139:41824

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